**Disodium disulphite**

*CAS N°: 7681-57-4*
SIDS Initial Assessment Report
for 13th SIAM
(Bern, 6-9 November 2001)

Chemical Name: Disodium disulphite

CAS No: 7681-57-4

Sponsor Country: Republic of Korea/ ICCA(BASF)

National SIDS Contact Point in Sponsor Country:
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History:
This HPV chemical was assigned to Korea in 1999. In 2000, ICCA (BASF) proposed to be co-sponsor and prepared the draft documents (Dossier, SIAR, SIAP). It was submitted to the SIDS Contact Point of Korea on Nov. 2000. The draft documents were revised by Korea after discussion with BASF. Robust Study Summaries were prepared according to the new RSS templates by Korea. The revised draft was sent to BASF for a detailed discussion on Aug 2001. In the meantime, Korea performed an acute toxicity test with fish. After agreement, the documents were finalized and the checklist was developed by Korea.

Testing:
No testing ( )
Testing ( x ) Acute toxicity to Fish

Comments:

Deadline for circulation:
Date of Circulation:

Revised : September 2001
**SIDS INITIAL ASSESSMENT PROFILE**

<table>
<thead>
<tr>
<th>CAS No.</th>
<th>7681-57-4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemical Name</strong></td>
<td>Disodium disulphite</td>
</tr>
</tbody>
</table>
| **Structural Formula** | \[
\begin{array}{c}
\text{Na}^+ \text{O} \backslash \text{S} \text{O} \\
\text{Na}^+ \text{O} \backslash \text{S} \text{O} \\
\end{array}
\] |

**RECOMMENDATIONS**

The chemical is currently of low priority for further work.

**SUMMARY CONCLUSIONS OF THE SIAR**

**Human Health**

Disodium disulphite is rapidly eliminated as sulphate in humans and dogs. When sulphite is present in the tissues in sufficiently high concentrations, it may be metabolized to inorganic thiosulphate that is then excreted in the urine. The acute toxicity of oral LD$_{50}$ in rats is 1,540 mg/kg bw. In decedents, toxicity was observed to the stomach and liver, and the gastro-intestinal tract was filled with blood. For repeated dose toxicity, disodium disulphite was given to rats through diet for 30 to 104 weeks. The predominant effect was the induction of stomach lesions due to local irritation and was characterized as forestomach and glandular stomach hyperplasias and inflammation. There were no signs of local toxicity (stomach irritation) at ca. 217 mg/kg bw/day, and the lowest dose where this effect occurred was ca. 454 mg/kg bw/day as actual intake dose [NOAEL for local (stomach irritation), rats, oral feed : ca. 217 mg/kg bw/day]. From the same dietary study in rats, the NOAEL for systemic effects was the highest dose tested (942 mg/kg bw/day).

The results of genotoxic tests *in vitro* are equivocal but there is no evidence that disodium disulphite is genotoxic *in vivo*. It was not carcinogenic in rats that received disodium disulphite via feed for 104 weeks. No reproduction toxicity of disodium disulphite was observed for a period of up to 2 years and over three generations (NOAEL, fertility, oral feed: ca. 942 mg/kg bw/day). No developmental toxicity and teratogenic effects appeared in rats or rabbits at the highest dose tested (NOAEL 110 and 123 mg/kg bw/day, respectively).

This chemical is not irritating to the skin, but irritating to the eyes. In humans, urticaria and asthma with itching, edema, rhinitis, and nasal congestion were reported. An immunological pathogenesis of these reactions is still not clear. In a non-guideline study, no indication of skin sensitization for guinea pig was observed. In a few cases allergic contact dermatitis as well as positive patch-testing was observed. With respect to wide spread use, it is not considered as a skin sensitizer. Disodium disulphite is unlikely to induce respiratory sensitization but may enhance symptoms of asthma in sensitive individuals. Given the wide-spread use, the number of cases is considered to be low.

**Environment**

Boiling point, melting point and vapour pressure are not relevant for disodium disulphite. Also, testing for the endpoint of biodegradability, is not appropriate due the chemical not being an organic chemical. Bioaccumulation is not expected. For the boiling point, decomposition occurred at 150 °C to form sulfur dioxide. This chemical will be mainly transported to the water compartment when released to environmental compartments since it is highly water soluble (470 g/L at 20° ). The b w K$_\text{OC}$ (2.447) indicates that disodium disulphite is so mobile in soil that it may not stay in the terrestrial compartment. Instead it has a potential to leach into the groundwater.

The chemical has been tested in a limited number of aquatic species. In an acute toxicity test with fish, the 96 hr-LC$_{50}$ was >100 mg/L. For algae, the 72 hr-EC$_{50}$ was 48.1 mg/L. For daphnids, the acute 48 hr-EC$_{50}$ was 88.76 mg/L.
and the chronic 21-day NOEC was >10 mg/L. Therefore, a PNEC of 0.1 mg/L for aquatic organisms was obtained from the chronic NOEC for daphnids using an assessment factor of 100.

**Exposure**

In 1999, estimates for the world market of sodium salts of sulphites, without China and the Russian Federation, amounted to approx. 330,000 tonnes/year. These are distributed as follows: 20,000 tonnes in Germany, 60,000 tonnes in the rest of Europe and 250,000 tonnes in the rest of the world. Disodium disulphite is a basic chemical and used in chemical synthesis. Exposure to consumer may occur, but the extent of this exposure is unknown. There is a potential for exposure to the respiratory tract, skin and eyes during manufacture or formulation of the chemical into products.

In Korea, the total production of disodium disulphite was about 3,200 tonnes/year in 1998. The chemical is used in tanning agents, food additives, bleaching agents, photography and reducing agents but the amount for each use pattern is not available. There is no exposure data for the environment and humans at the present time.

**NATURE OF FURTHER WORK RECOMMENDED**

No recommendation.
## FULL SIDS SUMMARY

### PHYSICAL-CHEMICAL

<table>
<thead>
<tr>
<th>Species</th>
<th>Protocol</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Melting Point</td>
<td>NA</td>
<td>150 °C (decomposes to form sulfur dioxide)</td>
</tr>
<tr>
<td>2.2 Boiling Point</td>
<td>-</td>
<td>Decomposed</td>
</tr>
<tr>
<td>2.3 Density</td>
<td>NA</td>
<td>1480 kg/m³</td>
</tr>
<tr>
<td>2.4 Vapour Pressure</td>
<td>-</td>
<td>Not relevant</td>
</tr>
<tr>
<td>2.5 Partition Coefficient (Log P&lt;sub&gt;OW&lt;/sub&gt;)</td>
<td>NA</td>
<td>-3.7 at 25 °C</td>
</tr>
<tr>
<td>2.6A Water Solubility</td>
<td>NA</td>
<td>470 g/L at 20 °C</td>
</tr>
<tr>
<td>B pH</td>
<td>NA</td>
<td>pH 3.5-5.0 (50 g/L) at 20 °C</td>
</tr>
<tr>
<td>2.12 Oxidation: Reduction Potential</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

### ENVIRONMENTAL FATE AND PATHWAY

<table>
<thead>
<tr>
<th>Environment</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1.1 Photodegradation</td>
<td>Not relevant</td>
</tr>
<tr>
<td>3.1.2 Stability in Water</td>
<td>Not relevant (Dissociates in water to sodium cations, disulfite anions and sulfur dioxide)</td>
</tr>
<tr>
<td>3.2 Monitoring Data</td>
<td>No data</td>
</tr>
<tr>
<td>3.3 Transport and Distribution</td>
<td>Not relevant</td>
</tr>
<tr>
<td>3.5 Biodegradation</td>
<td>Not relevant (inorganic compounds)</td>
</tr>
</tbody>
</table>

### ECOTOXICOLOGY

<table>
<thead>
<tr>
<th>Species</th>
<th>Protocol</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1 Acute/Prolonged Toxicity to Fish</td>
<td>Oryzias latipes</td>
<td>LC₅₀ (96 hr) &gt;100 mg/L</td>
</tr>
<tr>
<td></td>
<td>Salmo gairdneri</td>
<td>LC₅₀ (96 hr) &gt;147 mg/L and &lt; 215 mg/L</td>
</tr>
<tr>
<td>4.2 Acute Toxicity to Aquatic Invertebrates</td>
<td>Daphnia magna</td>
<td>EC₅₀ (48 hr) = 88.76 mg/L</td>
</tr>
<tr>
<td>4.3 Toxicity to Aquatic Plants e.g. Algae</td>
<td>Scenedesmus subspicatus</td>
<td>EC₅₀ (72 hr) = 48.1 mg/L</td>
</tr>
<tr>
<td>4.5.2 Chronic Toxicity to Aquatic Invertebrates</td>
<td>Daphnia magna</td>
<td>LC₅₀ (21 d) &gt; 10 mg/L NOEC (21 d) &gt; 10 mg/L</td>
</tr>
<tr>
<td>4.6.1 Toxicity to Soil Dwelling Organisms</td>
<td>-</td>
<td>No data</td>
</tr>
<tr>
<td>4.6.2 Toxicity to Terrestrial plants</td>
<td>-</td>
<td>No relevant data available</td>
</tr>
<tr>
<td>4.6.3 Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)</td>
<td>-</td>
<td>No data</td>
</tr>
</tbody>
</table>

### TOXICOLOGY

<table>
<thead>
<tr>
<th>Species</th>
<th>Protocol</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1.1 Acute Oral Toxicity</td>
<td>Rat</td>
<td>LD₅₀ = 1540 mg/kg</td>
</tr>
<tr>
<td>5.1.2 Acute Inhalation Toxicity</td>
<td>-</td>
<td>No data</td>
</tr>
<tr>
<td>5.1.3 Acute Dermal Toxicity</td>
<td>-</td>
<td>No data</td>
</tr>
<tr>
<td>5.2.1 Skin irritation</td>
<td>Rabbit</td>
<td>Not irritating</td>
</tr>
<tr>
<td>5.2.2 Eye irritation</td>
<td>Rabbit</td>
<td>Irritating</td>
</tr>
<tr>
<td>5.3 Skin sensitization</td>
<td>Guinea pig</td>
<td>Not sensitizing (Standardized skin sensitization test)</td>
</tr>
</tbody>
</table>

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**OECD SIDS DISODIUM DISULPHITE**

**CAS NO : 7681-57-4**

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<table>
<thead>
<tr>
<th>CAS NO : 7681-57-4</th>
<th>SPECIES</th>
<th>PROTOCOL</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.4 Repeated Dose</td>
<td>Rat</td>
<td>Other (multigeneration</td>
<td>NOAEL = 217 mg Na₂S₂O₅/kg bw/day (0.5% in the diet) for local toxicity</td>
</tr>
<tr>
<td>Toxicity</td>
<td></td>
<td>study)</td>
<td></td>
</tr>
<tr>
<td>5.5 Genetic Toxicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In Vitro A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacterial Test</td>
<td></td>
<td>S. typhimurium</td>
<td>Negative (With &amp; without metabolic activation)</td>
</tr>
<tr>
<td>(Gene mutation)</td>
<td></td>
<td>E. coli</td>
<td>Negative (With &amp; without metabolic activation)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. typhimurium</td>
<td>Positive (Without metabolic activation)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other (Ames assay)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B Non-Bacterial In</td>
<td>CHL</td>
<td>Other (cytogenetic)</td>
<td>Negative</td>
</tr>
<tr>
<td>Vitro Test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Chromosomal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aberrations)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.6 Genetic Toxicity</td>
<td>Rat</td>
<td>Other (cytogenetic)</td>
<td>No tumorigenesis</td>
</tr>
<tr>
<td>In Vivo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.7 Carcinogenicity</td>
<td>Rat</td>
<td>Other</td>
<td>NOAEL = 942 mg of Na₂S₂O₅/kg bw/day (2% in the diet)</td>
</tr>
<tr>
<td>5.8 Toxicity to</td>
<td>Rat</td>
<td>Other (multigeneration</td>
<td></td>
</tr>
<tr>
<td>Reproduction</td>
<td></td>
<td>study)</td>
<td></td>
</tr>
<tr>
<td>5.9 Developmental</td>
<td>Rat</td>
<td>Other</td>
<td>NOAEL = 110 Na₂S₂O₅ mg/kg bw/day</td>
</tr>
<tr>
<td>Toxicity/</td>
<td>Rabbit</td>
<td>Other</td>
<td>NOAEL = 123 Na₂S₂O₅ mg/kg bw/day</td>
</tr>
<tr>
<td>Teratogenicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.11 Experience with</td>
<td>human</td>
<td>Patch test (dermatitis)</td>
<td>Positive</td>
</tr>
<tr>
<td>Human Exposure</td>
<td></td>
<td>Patch-tests (ocular</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>hypersensitivity)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inhalation, ingestion</td>
<td>Asthma, anaphylaxis</td>
</tr>
</tbody>
</table>
1. IDENTIFY

- **OECD Name**: Disodium disulphite
- **Synonym**: Dinatriumdisulfite, Disodium disulphite, Disodium metabisulfite, Disodium pyrosulfite, Disulfurous acid, disodium salt (9CI), Natriumsulfite, Pyrosulfurous acid, disodium salt (8CI), Sodium disulfite, Sodium metabisulfite, Sodium pyrosulfite
- **CAS Number**: 7681-57-4
- **Molecular Formula**: \( \text{Na}_2\text{S}_2\text{O}_5 \)
- **Structural Formula**:

  ![Structural Formula](image)
- **Degree of Purity**: > 98 % w/w
- **Physical-chemical properties**
  - **Melting Point**: 150 °C (decomposition)
  - **Boiling Point**: -
  - **Vapour Pressure**: -
  - **Water Solubility**: 470 g/L at 20°
  - **Log Pow**: -3.7 at 25°
- **Classification in member countries**
  Not classified as a toxic chemical in the Toxic Chemicals Control Act, Republic of Korea
2. GENERAL INFORMATION ON EXPOSURE

In 1999, the estimates of the world market for sodium salts of sulfites without China and Russian Federation amounted to approx. 330,000 tonnes/year. These are distributed as follows: 20,000 tonnes in Germany, 60,000 tonnes in the rest Europe and 250,000 tonnes in the rest of the world. Disodium disulphite is a basic chemical and used in synthesis. It is also used in tanning agents, food/foodstuff additives, bleaching agents, photography, etc. Total production of disodium disulphite in Korea was about 3,200 tonnes/year in 1998 (MOE, Korea, 1998). There is no exposure data for the environment and humans at the present time.

2.1 Environmental Fate

Testing for the endpoint of biodegradability is not appropriate due the chemical not being an organic chemical. Also, bioaccumulation is not expected. The product may lead 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. The substance can release sulphur dioxide under acid conditions, but this is not likely to occur under normal natural environmental conditions.

Disodium disulphite dissolves in water and forms sodium cations, disulfite anions, and sulfur dioxide. Depending on the pH-value, sulfur dioxide, sodium hydrogen sulfite or sodium sulfite are present in the aqueous solution.

Photodegradation of disodium disulphite in water is not relevant because it is quickly ionized in water.

The evaluation of the fugacity model for disodium disulphite is not relevant because it is an inorganic chemical, very soluble in water (470 g/L)

2.2 Human Exposure

Exposure to consumers may occur but the extent of this exposure is unknown. Several occupational and consumer exposure cases have been reported. An occupational asthma in laundry workers (Le-Stradic-Reygagne, 1991), dermatitis and asthma in a photographic technician (Jacobs et al, 1992), occupational bronchospasm (Vallon et al., 1995), a case of asthma after ingesting a disodium disulphite containing salad (Baker et al., 1981) and a case of intermittent urticaria (Wuethrich et al., 1993) indicate that this chemical could have an impact on sensitive individuals. No data is available regarding human exposure in Korea.
3. HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics & Metabolism

It was stated that a rapid and quantitatively elimination of disodium disulphite as sulfate was observed in man and dog (Rost, 1993). When sulphite is present in the tissues in sufficiently high concentrations, it may be metabolized to inorganic thiosulphate excreted in the urine. Sulphite may damage DNA chains, presumably by a reaction involving free radicals. However, mammalian tissues are largely protected against hazards from sulphite by its oxidation to the relatively non-toxic sulphate (Renner, 1983).

3.1.2 Acute Toxicity

Acute toxicity data are reported in literature for rats and other species. Oral LD₅₀ of 1540 and 2480 mg/kg bw in rats have been reported (Hoechst AG, 1987; NTIS, 1972). The acute LD₅₀ by oral exposure in rat is 1540 mg/kg bw and deaths were observed at 1250 mg/kg and above. In the dead animals, the following gross observations were seen; the gastro-intestinal tract was filled with blood, reddened mucosa of the stomach and the dark colored liver, but unusual gross abnormalities were not found in surviving rats (Hoechst AG, 1987).

Conclusion:

The acute oral LD₅₀ in rats is 1540 mg/kg bw. In decedents, toxicity was observed to the stomach, liver and the gastro-intestinal tract was filled with blood.

3.1.3 Repeated Dose Toxicity

An assessment of repeated dose toxicity was performed using a multigeneration study with Wistar rats (Til et al., 1972). Rats were exposed to disodium disulphite in a supplemented diet with thiamine (ca. 2 mg/kg bw) since sulfites are known to break down thiamine. Twenty animals/dose/sex received a diet containing 0, 0.125, 0.25, 0.5, 1.0 or 2.0 % of disodium disulphite (i.e. actual doses of ca. 48, 106, 217, 454, and 942 mg/kg/day) for 104 weeks (F₀- and F₁-generations) or for 30 weeks (F₂-generation).

The general condition of the animals was good during the first 72 weeks of the F₀-generation, as was the case in the next generation. Overall, survival in the sulphite groups was generally higher than in the controls, except in the case of males of the F₁-generation given 2 % sulphite. However, no deaths occurred in the females of the same dose group. The body weights of the F₀-generation were comparable in all groups irrespective of treatment. There was a marginal reduction in body weight gain in both sexes of F₁-and F₂-generation rats given 2 % disodium disulphite.

A marginally reduced hemoglobin content, hematocrit and erythrocyte count occurred in F₀-generation males at the 2 % dose at week 52, 78 and 100, and the F₁-generation males at 2 % showed an increase in leukocyte count at week 102. All rats in the highest dose group showed indications of occult blood in the feces of all generations; this also occurred at other doses, however, only sporadically.

Pathological changes attributable to feeding sulfites were only observed in the stomach. A raised and thickened limiting ridge and small amounts of a reddish brown flocy material in the mucus layer of the glandular stomach were seen grossly in the two highest doses. Lesions were microscopically characterized as forestomach and glandular stomach hyperplasia or inflammation, and were seen mostly in the 1 and 2 % dose groups (seen mainly at 2 years in the F₀- and F₁-
generation, and at 30 weeks in the F2-generation). At the 0.5 % dose, a few forestomach lesions were seen in the F2-generation rats. Other non-neoplastic lesions observed in treated groups were comparable to controls. In section 3.1.5 information on neoplastic changes are reported. No histologic changes were noted in the gonads. Section 3.1.6 of this SIAR describes the reproductive effects seen in this experiment.

In summary, no signs of systemic toxicity were observed. Therefore, the NOAEL for systemic toxicity was the highest dose tested. The only major finding in this study was local irritation in the stomach. The repeated dose where no stomach irritation occurred in the F0-generation was 0.5 % in the diet. Taking the loss of sulphite into account, the actual dose was 0.44 % Na2S2O5 that is equivalent to an intake of 217 mg Na2S2O5 /kg bw/day. The lowest dose where local effects occurred in the F0-generation was 1.0 % in the diet that is equivalent to an intake of 454 mg Na2S2O5/kg bw/day.

Conclusion:
Disodium disulphite primarily caused stomach lesions due to local irritation under the conditions of the present study. There were no signs of local toxicity at ca. 217 mg/kg bw/day, and the lowest dose where this effect occurred was ca. 454 mg/kg bw/day as actual intake dose (NOAEL & LOAEL for local toxicity, rats, oral feed: ca. 217 mg/kg bw/day & 454 mg/kg bw/day). From the same dietary study in rats, the NOAEL for systemic toxicity was the highest dose tested (NOAEL for systemic toxicity, rats, oral feed: ca. 942 mg/kg bw/day).

3.1.4 Genetic Toxicity

Genetic Toxicity in vitro
Disodium disulphite was not mutagenic in the Ames assay performed with and without S-9 mix, using both standard plate and preincubation test conditions (NTIS, 1978; BASF AG, 1989). Nor did it induce chromosomal aberrations in a Chinese hamster fibroblast cell line (Ishidate et al., 1984). However, there were other in vitro bacterial assays with positive results (Pagano and Zeiger, 1987; Pagano et al., 1990; De Giovanni-Donelly, 1985). Sensitivity to mutation by bisulfite was shown in strains which carried cytosines in the appropriate context in the putative target region of DNA, since bisulfite has been suggested to cause cytosine deamination in single stranded DNA. In summary they mentioned that bisulfite was a weak mutagen in bacteria when cytosines were found as CCC and CCCCCC runs, but not in CCCC or GC runs (De Giovanni-Donelly 1985, Pagano and Zeiger 1987). These positive results also suggest that the SO3- radical is responsible for the mutagenic activity (Pagano et al., 1990) and clearly depends on the specific test condition such as pH value. The proper pH range (pH 4.4 to 5.6) for mutagenicity was also determined (Pagano and Zeiger 1987). However, their doses were not clearly presented. If very high doses were used, the positive effects could be attributed to an impurity. No data on purity was given. These positive in vitro studies referred above could not support that the substance is clearly genotoxic since the free radical-mediated mutagenic effects are generally very transient. Moreover, such mutagenic mechanism does not seem to be relevant to in vivo condition where the autooxidation of disodium disulphite occurred (Renner 1983).

Genetic Toxicity in vivo
No adverse effect on bone marrow chromosomes was observed in rats as a result of disodium disulphite treatment by gavage (NTIS, 1972 and Maxwell et al., 1974). Likewise, an evaluation for mutagenicity in a dominant lethal assay showed no substance-related effect attributable to disodium disulphite given by feed (NTIS, 1979).

Conclusion:
The genetic toxicity of this chemical is equivocal in vitro but the substance is not genotoxic under in vivo condition.
3.1.5. Carcinogenicity

The study described in section 3.1.3 (disodium disulphite given in the diet with 0.125, 0.25, 0.5, 1.0, 2.0 %, i.e. ca. 48, 106, 217, 454, and 942 mg/kg/day as actual dose and supplemented with thiamine due to its breakdown by sulphite) using rats by Til et al. (1972) is not a conventional carcinogenicity study as the animals were mated to determine reproductive performance. Nevertheless, this data is sufficient to assess the carcinogenic potential of disodium disulphite since animals were maintained for 104 weeks, the usual time frame for a carcinogenicity bioassay, and suitable histologic examinations were performed. In this regard, the number of lymphoreticular pulmonary tumors in males decreased with increasing levels of sulphite. The incidence of thyroid and pituitary tumors in control males was exceptionally low, whereas those noted in the various test groups represented numbers normally found in the strain of Wistar rats used. All other neoplasms occurred in a sporadic manner with no apparent relationship between number, location or type of tumors and the treatment.

Conclusion:
Disodium disulphite was not carcinogenic to rats.

3.1.6. Reproduction Toxicity

As described in section 3.1.3, rats were treated with 0, 0.125, 0.25, 0.5, 1.0 and 2.0 % of disodium disulphite (ca. 0, 48, 106, 217, 454, and 942 mg/kg bw/day actual doses) in a supplemented diet with thiamine, since sulphites are known to break down thiamine (Til et al., 1972). The F0-generation was mated at week 21 of treatment. Half of the animals were mated again at week 34. Animals from the 1st litter were selected at weaning to become the F1a-generation. The F1a-generation was mated at weeks 12 and 30 to produce F2a- and F2b-generations. Animals from the F2a litters were mated to produce F3a- and F3b-generations by pairing on weeks 14 and 22.

Body weight was not reduced in any treatment group in the F0-generation. There was a marginal reduction in body weight in both sexes of the 2 % group in the F1- and the 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 the F1b-generation offspring (F2a and F2b pups) dietary levels of 1 and 2 % disodium disulphite 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 the control groups. Furthermore, these body weight changes were within or were not dramatically different from the control values of the F1 pups. 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 reproduction toxicity was the highest dose 2 % in the diet that is equivalent to 942 mg/kg bw/day as actual dose.

Conclusion:
There is no suggestive evidence of reproductive toxicity in rats that received orally 942 mg/kg bw/day of disodium disulphite as actual dose (2 % in the diet). The NOAEL (rat, fertility, F0, F1, F2, F3, oral feed) was 942 mg/kg bw/day.
3.1.7. Developmental Toxicity

When pregnant Wistar rats were exposed to 0, 1, 5, 24, 110 mg/kg bw/day by gavage for 6-15 days of gestation (NTIS, 1972), disodium disulphite had no effect on nidation, on maternal and fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the numbers occurring in the sham-treated controls. Thus, the NOAELs for maternal toxicity and teratogenicity as well as embryo/fetotoxicity were the highest dose tested.

- NOAEL, rats, maternal toxicity, oral: 110 mg/kg bw/day
- NOAEL, rats, teratogenicity, oral: 110 mg/kg bw/day
- NOAEL, rats, embryo/fetotoxicity, oral: 110 mg/kg bw/day

Pregnant rabbits (Dutch-belted) were treated by gavage on days 6-18 of gestation with 0, 1.23, 5.71, 26.5 or 123 mg/kg bw/day of disodium disulphite, and were sacrificed on day 29 (NTIS, 1974). Again, the test substance had no clear effect on nidation, or on maternal or fetal 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. The NOAELs for maternal toxicity, teratogenicity and embryo/fetotoxicity were the highest dose tested.

- NOAEL, rabbits, maternal toxicity, oral: 123 mg/kg bw/day
- NOAEL, rabbits, teratogenicity, oral: 123 mg/kg bw/day
- NOAEL, rabbits, embryo/fetotoxicity, oral: 123 mg/kg bw/day

Conclusion:

Disodium disulphite showed no evidence of developmental toxicity or teratogenicity. The NOAELs were established at 110 mg/kg bw/day in rats and 123 mg/kg bw/day in rabbits, respectively.

3.1.8. Other: Irritation (Human data); Sensitisation; Corrosivity

There are only a few animal studies relating to irritation of disodium disulphite. These two studies show disodium disulphite is not irritating to the skin but irritating to the eyes of rabbits (Hoechst AG, 1987). Regarding skin sensitization in animals, no guideline studies were available for an assessment, however, in one study with guinea pigs which was not well-documented, no indication of sensitization was observed. In humans urticaria and asthma with itching, edema, rhinitis, and nasal congestion are reported (Le-Stradic-Reygagne, 1991; Baker, 1981; Vallon, 1995; Valero, 1993; Sanz, 1992; Wüthrich et al., 1993). An immunological pathogenesis of these are not still clear. In a few cases allergic contact dermatitis, as well as positive patch-testing was observed (Jacobs, 1992; Apetato, 1986; Sokol, 1990; Petersen, 1990; Larame, 1989; Vestergaard and Andesen, 1995).

Conclusion:

Disodium disulphite is not irritating to the skin but irritating to the eyes. It is not considered as skin sensitizer and also unlikely to induce respiratory sensitization but may enhance symptoms of asthma in sensitive individuals.

3.2 Initial Assessment for Human Health

Acute toxicity of disodium disulphite is likely to be low since the LD_{50} by oral exposure in rat is 1540 mg/kg bw. This chemical is not irritating to the skin, but irritating to the eyes with risk of serious damage.

For repeated dose toxicity, in long term dietary studies (30 to 104 weeks) in rats, the predominant effect was the induction of stomach lesions due to local irritation and was characterized as
forestomach and glandular stomach hyperplasias and inflammation. There were no signs of local toxicity at ca. 217 mg/kg bw/day, and the lowest dose where this effect occurred was ca. 454 mg/kg bw/day as actual intake dose (NOAEL for local toxicity: ca. 217 mg/kg bw/day). From the same dietary study in rats, the NOAEL for systemic toxicity was the highest dose tested (NOAEL, rats, oral feed: ca. 942 mg/kg bw/day).

The results of genotoxic tests in vitro are equivocal but there is no evidence demonstrating that disodium disulphite is genotoxic in vivo.

Reproduction toxicity of disodium disulphite was not observed (NOAEL, rats, fertility, oral feed: ca. 942 mg/kg bw). No developmental toxicity and teratogenic effects were observed in rats or rabbits (NOAEL, rats, maternal toxicity/teratogenicity/embryo/fetotoxicity, oral: 110 mg/kg bw; NOAEL, rabbits, maternal toxicity/teratogenicity/embryo/fetotoxicity, oral: 123 mg/kg bw).

It was not carcinogenic in rats that received disodium disulphite via feed.

In humans, urticaria and asthma with itching, edema, rhinitis and nasal congestion were reported. An immunological pathogenesis of these reactions is not still clear. In a non-guideline study, no indication of skin sensitization with guinea pigs was observed. In a few cases allergic contact dermatitis as well as positive patch-testing was observed. With respect to wide spread use, it is not considered as a skin sensitizer. Disodium disulphite is unlikely to induce respiratory sensitization but may enhance symptoms of asthma in sensitive individuals. Given the wide-spread use, the number of cases is considered to be low.
4. HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

The following acute toxicity tests with aquatic organisms were available:
Medaka (*Oryzias latipes*) : LC$_{50}$ (96 h) >100 mg/L, nominal concentration (MOE, Korea 2001)
Rainbow trout (*Salmo gairdneri*) : LC$_{50}$ (96 hr) >147 mg/L and <215 mg/L, nominal concentration (BASF, 1981)
Water flea (*Daphnia magna*) : EC$_{50}$ (48 h) = 88.76 mg/L, nominal concentration (BASF, 1989)
Algae (*Scenedesmus subspicatus*) : EC$_{50}$ (72 h) = 48.1 mg/L, nominal concentration (BASF, 1989)
Bacteria (*Pseudomonas putida*) : EC$_{50}$ (17 h) = 56.1 mg/L, nominal concentration (BASF, 1988)
The following chronic toxicity test with aquatic organisms was available:
Water flea (*Daphnia magna*) : 21d-NOEC > 10 mg/L (BASF, 1993). The test concentrations were 1, 5, and 10 mg/L.

4.2 Terrestrial Effects

There is almost no data available on the terrestrial organisms. A study showed that treatment of tomato leaves with different concentrations of disodium disulphite induced degradation of green pigments and protein. The author suggested that SO$_2$ might be responsible for the decreased protein content of treated leaves. However, the value of K$_{OC}$ (2.477) is low implying that it is very mobile in soil. Therefore given the low potential for exposure in terrestrial compartment, significant toxicity in terrestrial organism is unlikely.

4.3 Other Environmental Effects

There is no available information.

4.4 Initial Assessment for the Environment

Testing for the endpoint of biodegradability is not appropriate due the chemical not being an organic chemical. Also, bioaccumulation is not expected. As mentioned above, the low K$_{OC}$ (2.447) indicates that disodium disulphite is so mobile in soil that it may not stay in the terrestrial compartment. Instead it has a potential to leach into the groundwater.

From the experimental acute toxicity result of the most sensitive organism, 48.1 mg/L (72 hr-EC$_{50}$ for algae; *Scenedesmus subspicatus*), an assessment factor 100 was applied to determine PNEC of 0.481 mg/L. From a chronic toxicity value of > 10 mg/L (21days-NOEC for *Daphnia magna*), a PNEC of 0.1 mg/L was derived by applying an assessment factor of 100. Therefore the lowest PNEC was determined to be 0.1 mg/L.
5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

Physical/Chemical property, production, use and distribution

In 1999, estimates for the world market of sodium salts of sulphites, without China and the Russian federation, amounted to approx. 330,000 tonnes/year. Total production of disodium disulphite in Korea was about 3,200 tonnes/year. Disodium disulphite is a basic chemical and used in synthesis. The substance is also used in tanning agents, food/foodstuff additives, bleaching agents, photography, etc.

Environment

The estimated distribution shows water is the main target compartment for disodium disulphite. The substance has no considerable potential for bio- and geoaccumulation (logPow-3.7, measured). Biodegradation or elimination tests may not be appropriate since disodium disulphite is an inorganic substance. Disodium disulphite dissolves in water and forms sodium cations, disulfite anions, and sulfur dioxide. Photodegradation is not relevant under environmental conditions.

The following acute toxicity tests with aquatic organisms were available:

- Medaka (*Oryzias latipes*): LC$_{50}$ (96 h) >100 mg/L, nominal concentration (MOE, Korea, 2001)
- Rainbow trout (*Salmo gairdneri*): LC$_{50}$ (96 hr) >147 mg/L and <215 mg/L, nominal concentration (BASF, 1981)
- Water flea (*Daphnia magna*): EC$_{50}$ (48 h) = 88.76 mg/L, nominal concentration (BASF, 1989)
- Algae (*Scenedesmus subspicatus*): EC$_{50}$ (72 h) = 48.1 mg/L nominal concentration (BASF, 1989)
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The following chronic toxicity test with aquatic organisms was available:

- Water flea (*Daphnia magna*): 21d-NOEC > 10 mg/L (BASF, 1993). The test concentrations were 1, 5, and 10 mg/L.

From a chronic toxicity value of 10 mg/L (21days-NOEC of *Daphnia magna*), a PNEC of 0.1 mg/L was derived by applying an assessment factor of 100.

Human Health

Acute toxicity of disodium disulphite is likely to be low since the LD$_{50}$ for oral exposure in rats is 1540 mg/kg bw. This chemical is not irritating to the skin, but irritating to the eyes with risk of serious damage.

In long term dietary studies (30 to 104 weeks) in rats, the predominant effect was the induction of stomach lesions due to local irritation and was characterized as forestomach and glandular stomach hyperplasias and inflammation. There were no signs of local toxicity at ca. 217 mg/kg bw/day, and the lowest dose where this effect occurred was ca. 454 mg/kg bw/day as actual intake dose (NOAEL for local toxicity: ca. 106 mg/kg bw/day) in the F0 generation. From the same dietary study in rats, the NOAEL for systemic toxicity was the highest dose tested (NOAEL, rats, oral feed: ca. 942 mg/kg bw/day).

The results of genotoxic tests *in vitro* are equivocal but there is no evidence that disodium disulphite is genotoxic *in vivo*.

Reproductive toxicity of disodium disulphite was not observed (NOAEL, rats, fertility, oral feed: ca. 942 mg/kg bw). No developmental toxicity or teratogenic effects appeared in rats or rabbits (NOAEL, rats, maternal toxicity/teratogenicity/embryo/fetotoxicity, oral: 110 mg/kg bw; NOAEL, rabbits, maternal toxicity/teratogenicity/embryo/fetotoxicity, oral: 123 mg/kg bw). It was not carcinogenic in rats that received disodium disulphite via feed.

In humans, urticaria and asthma with itching, edema, rhinitis, and nasal congestion have been reported. An immunological pathogenesis of these reactions is still unclear. In a few cases allergic contact dermatitis as well as positive patch-testing was observed. Given the wide-spread use, the
number of cases is considered to be low.

5.2 Recommendations

The chemical is currently of low priority for further work.
6. REFERENCES

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SIDS DOSSIER

Disodium Disulphite

CAS No. 7681-57-4

Sponsor Country: Republic of Korea/ICCA(BASF)

DATE: September 2001
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SID S SUMMARY

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C. NAME (OECD NAME)
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| 1.2 | OTHER CHEMICAL IDENTITY INFORMATION | Dinatriumdisulfit  
Disodium disulphite  
Disodium metabisulfite  
Disodium pyrosulfite  
Disulfurous acid, disodium salt (9CI)  
Natriumdisulfit  
Pyrosulfurous acid, disodium salt (8CI)  
Sodium disulfit  
Sodium metabisulfit  
Sodium pyrosulfit |
| 1.5 | QUANTITY | 100 000 - 500 000 tonnes per annum (World)  
1,000-5,000 tonnes per annum (Korea) |
| 1.7 | USE PATTERN | Wide-dispersive use  
(tanning agents, food/foodstuff additives, bleaching agents, photography, etc.) |
| 1.9 | SOURCES AND LEVELS OF EXPOSURE | |
| ISSUES FOR DISCUSSION (IDENTIFY, IF ANY) | |
## SIDS SUMMARY

**CAS NO:** 7681-57-4

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**ENVIRONMENTAL FATE and PATHWAY**

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| 3.3 Transport and Distribution |     |     |     |     |     |     |     |     |
| 3.5 Biodegradation |     |     |     |     |     |     |     |     |

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**ECOTOXICITY**

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| 4.2 Acute toxicity to Daphnia | Y   | N   | N   | Y   | N   | Y   | N   |     |
| 4.3 Toxicity to Algae | Y   | Y   | N   | N   | N   | Y   | N   |     |
| 4.5.2 Chronic toxicity to Daphnia | Y   | Y   | Y   | N   | N   | Y   | N   |     |
| 4.6.1 Toxicity to Soil dwelling organisms | N   |     |     |     |     |     |     |     |
| 4.6.2 Toxicity to Terrestrial plants | Y   |     |     |     |     |     |     |     |
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**OTHER ECOTOXICITY STUDIES RECEIVED**

**TOXICITY**

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**OTHER TOXICITY STUDIES RECEIVED**
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

A. CAS number  7681-57-4

B. Name (IUPAC name)  Disodium disulphite

C. Name (OECD name)  Disodium disulphite (EINECS)

D. CAS Descriptor

    Not Applicable since disodium disulphite is not a complex chemical.

E. EINECS-Number  231-673-0

F. Molecular Formula  $\text{Na}_2\text{S}_2\text{O}_5$

G. Structural Formula

\[
\text{Smiles Code} : [\text{Na}][\text{OS}(-\text{O})][-\text{O}]\text{S}(-\text{O})\text{O}[\text{Na}]
\]

H. Substance Group

    Not applicable

I. Substance Remark (Indicate the substance remark as prescribed in the EINECS Inventory, if possible)

    Not applicable since no prescription in the EINECS Inventory.

J. Molecular Weight  190.10

1.02 OECD INFORMATION

A. Sponsor Country:  Republic of Korea/ICCA (BASF)

B. Lead Organisation:

    Name of Lead Organisation: National Institute of Environmental Research
    Contact person:  Dr. Moon-Soon LEE
    Address:  Street: Gyeongseo-dong, Seo-gu
              Postal code  404-170
              Town:  Incheon
              Country:  Republic of Korea
              Tel:  82-32-560-7113
              Fax:  82-32-568-2037
              E-mail:  mslee416@me.go.kr

C. Name of responder  (Information on a responder should be provided when companies respond to Lead

    Organisation or SIDS Contact Points.)

    Name :  same as above
    Address :  same as above
1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance
   element [ ]; inorganic [x]; natural substance [ ]; organic [ ];
   organometallic [ ]; petroleum product [ ]

B. Physical State (at 20 °C and 1.013 hPa)
   gaseous [ ]; liquid [ ]; solid [x]

C. Purity
   > 98 % w/w

1.2 SYNONYMS

   Dinatriumdisulfit
   Disodium disulphite
   Disodium metabisulfite
   Disodium pyrosulfite
   Disulfurous acid, disodium salt (9CI)
   Natriumdisulfit
   Pyrosulfurous acid, disodium salt (8CI)
   Sodium disulfite
   Sodium metabisulfite
   Sodium pyrosulfite

1.3 IMPURITIES

   [Indicate CAS No., chemical name (IUPAC name is preferable), percentage, if possible EINECS number.]

   CAS No: 
   EINECS No:  
   Name: Cl- 
   Value: Less than 0.05 %
   Remarks: 

   CAS No: 
   EINECS No: 
   Name: S$_2$O$_3$2- 
   Value: Less than 0.05 %
   Remarks:  

   CAS No: 
   EINECS No: 
   Name: heavy metals 
   Value: Less than 0.001 %
   Remarks: 

   CAS No: 
   EINECS No: 
   Name: Fe 
   Value: Less than 0.002 %
   Remarks: 

   CAS No: 
   EINECS No: 
   Name: Insolubles 
   Value: Less than 0.005 %
   Remarks: 
1.4 ADDITIVES (e.g. stabilising agents, inhibitors etc. Indicate CAS No., chemical name (IUPAC name is preferable), percent age, if possible EINECS number), the component of the UVCB (substance with no defined composition) should be indicated here.)

<table>
<thead>
<tr>
<th>CAS No:</th>
<th>EINECS No:</th>
<th>Name:</th>
<th>Value:</th>
<th>Remarks:</th>
</tr>
</thead>
</table>

1.5 QUANTITY [Information on production or import levels should be provided in figures or ranges (e.g. 1,000-5,000, 5,000-10,000 tonnes, etc.) per responder or country and the date for which those ranges apply should be given. For EU Member states, only indicate the EU import figure. Give an estimation of the global production quantity in the remarks field. Information on the number of producers in the country and the source of information should also be given in the remarks field.]

Estimated production
- World wide: 100,000 – 500,000 tonnes per annum (1999)
- Korea: 3,200 tonnes per annum (MOE, 1998)

Remarks: (If possible, indicate if the substance was produced and/or imported during the 12 months following adoption of the EU regulation on existing chemicals.)


1.6 LABELLING AND CLASSIFICATION [If possible, enter information on labelling and classification, such as labelling and classification system, existence of specific limit, symbols, nota, R-Phrases and S-Phrases of EC Directive 67/548/EEC. See HEDSET Explanatory Note.]

Labelling
Type:
Specific limits:
Symbols:
Nota:
R-phrases:
S-phrases:
Text of S-phrases:
Remarks:

Classification
Type:
Category of danger:
R-phrases:
Remarks:

*Disodium disulphite is not classified as toxic chemicals in Korea

1.7 USE PATTERN

A. General [Data on use pattern have to be given by assigning main types according to their exposure relevance (i.e. non-dispersive use, use in closed systems, use resulting in inclusion into or onto matrix and wide dispersive use), industrial categories (e.g. basic chemical industry, chemical industry, agricultural industry, personal and domestic use) and use categories such as colouring agents, intermediates, solvents, adhesives, cleaning/washing agents, fertilizers, impregnation agents, surface-active, etc. If available, give an estimation of different uses in percentage terms.]

<table>
<thead>
<tr>
<th>Type of Use:</th>
<th>Category:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) main</td>
<td>Wide dispersive use</td>
</tr>
<tr>
<td>industrial</td>
<td>Chemical Industry</td>
</tr>
</tbody>
</table>
OECD SIDS          DISODIUM DISULPHITE

(b) main Non dispersive use
    industrial Personal and domestic use
    use Food/foodstuff additives

(c) main Non dispersive use
    industrial Personal and domestic use
    use Bleaching agents

(d) main Non dispersive use
    industrial Personal and domestic use
    use Photography

Remarks: General use of Disodium disulphite in the world are shown above. Among 3,200 tonnes consumed in Korea, most of them are used for Tanning agents, Food/foodstuff additives. Information of other use is not available.


B. Uses in Consumer Products (If the chemical is present in consumer products as marketed give details of form of products function (e.g. detergent etc.), and percent in product and physical state of product as marketed (e.g. aerosol, powder or liquid))

<table>
<thead>
<tr>
<th>Function</th>
<th>Amount present</th>
<th>Physical state</th>
</tr>
</thead>
</table>

Remarks: Information of other use is not available.

Reference:

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE (Indicate the type of occupational exposure limit value including short-term exposure limit value. If a value does not exist, give the hygiene standard of the producer company if available. See also 5.11.)

Exposure limit value
Type: TLV (KO)
Value: 5 mg/m³ (8 hr TWA)

Short term exposure limit value
Value: Length of exposure period
Frequency:
Remarks:

Exposure limit value
Type: TLV (US)
Value: 5 mg/m³

Short term exposure limit value
Value: Length of exposure period
Frequency:
Remarks:
Reference: ACGIH Documentation of the TLV and Biological Exposure Indices (1991)

Exposure limit value
Type: REL (US)
Value: 5 mg/m³ (10 hr TWA)

Short term exposure limit value
Value: Length of exposure period
Frequency:
Remarks:
Reference: NIOSH pocket guide to chemical hazards (1994)
1.9 SOURCES OF EXPOSURE

Describe sources of potential human [other than concentration of chemicals in the workplace and indoor environment (see 5.11)], or environmental exposure, including emission data (e.g. quantities per media with information such as time dimensions of release, indication of type of release (e.g. point source or diffuse), type of estimating (e.g. average or worst case), uncertainties in estimation), for all phases of the life cycle of the chemical, if available, including manufacturing and user areas.

For environmental exposure, indicate the production process briefly, number of sites of manufacture and, the basis for concluding that the process is “closed” if applicable.

Also an indication of measured exposure levels (expressed in an appropriate form, e.g. geometric mean and standard deviation) can be mentioned here. Any information that will help to focus the assessment of exposure (either quantitative or qualitative in nature) can be mentioned, if available.

Source:

Remarks: the most probable human exposure would be occupational exposure, which may occur through dermal contact at workplaces.


1.10 ADDITIONAL REMARKS

A. Options for disposal [Mode of disposal (e.g. incineration, release to sewage system, etc.) for each category and type of use, if appropriate; recycling possibility]

Remarks:

Reference:

B. Other remarks

Remarks:

Reference:
2. PHYSICAL-CHEMICAL DATA

2.1 MELTING POINT (If more than one, identify the recommended value.)

Value:
Decomposition: Yes [x] No [ ] Ambiguous [ ]
Sublimation: Yes [ ] No [ ] Ambiguous [ ]
Method: GLP: Yes [ ] No [ ] ?[x]
Remarks: Solid temperature 150 °C (decompose to form sulfur dioxide)
Reference: BASF AG safety data sheet sodium metabisulfite, 06. January. 1999

2.2 BOILING POINT (If more than one, identify the recommended value.)

Value:
Pressure: 
Decomposition: Yes [x] No[ ] Ambiguous [ ]
Method: GLP: Yes [ ] No [ ] ?[x]
Remarks: not relevant (decomposition)
Reference:

2.3 DENSITY (relative density) (Where applicable, indicate the relative density of the substance.)

Type: Relative Density
Value: 1.48 g/cm³
Temperature: 15 °C
Method: GLP: Yes [ ] No [ ] ?[x]
Remarks:
Reference: BASF AG safety data sheet sodium metabisulfite, 06. January. 1999

2.4 VAPOUR PRESSURE (if more than one, identify the recommended value)

Value:
Temperature: °C
Method: GLP: Yes [ ] No [ ] ?[ ]
Remarks: not relevant
Reference:

2.5 PARTITION COEFFICIENT log POW (if more than one, identify the recommended value)

Log POW: -3.7
Temperature: 25 °C
Method: calculated [ ]; measured [x]
GLP: Yes [ ] No [ ] ?[x]
Remarks: log POW strongly depend on pH value

2.6 WATER SOLUBILITY (if more than one, identify the recommended value)

A. Solubility
a) Preferred result
Value: 470 g/l
Temperature: 0 °C
Description: Miscible[ ]; Of very high solubility [ ]; Of high solubility [x]; Soluble [ ]; Slightly soluble [ ]; Of low solubility [ ]; Of very low solubility [ ]; Not soluble

Method
GLP: Yes [ ] No [ ] ?[x]
Remarks:

b) Value: 640 g/l
Temperature: 25 °C
Description: Miscible[ ]; Of very high solubility [ ]; Of high solubility [x]; Soluble [ ]; Slightly soluble [ ]; Of low solubility [ ]; Of very low solubility [ ]; Not soluble

Method
GLP: Yes [ ] No [ ] ?[x]
Remarks:

c) Value: 540 g/l
Temperature: 25 °C
Description: Miscible[ ]; Of very high solubility [ ]; Of high solubility [x]; Soluble [ ]; Slightly soluble [ ]; Of low solubility [ ]; Of very low solubility [ ]; Not soluble

Method
GLP: Yes [ ] No [ ] ?[x]
Remarks:

B. pH Value, pKa value

pH Value: 3.5-5.0
Concentration: 50 g/l
Temperature: 20 °C
Method:
GLP: Yes [ ] No [ ] ?[x]
pKa value:
Remarks:

2.10 EXPLOSIVE PROPERTIES

Results: Explosive under influence of a flame[ ]; More sensitive to friction than m-dinitrobenzene [ ]; More sensitive to shock than m-dinitrobenzene [ ]; Not explosive [x]; Other [ ]
Method:
GLP: Yes [ ] No [ ] ?[x]
Remarks: because of chemical structure
Reference: BASF AG, Sicherheitstechnik, interne Mitteilung, 29.October.1999

2.11 OXIDIZING PROPERTIES

Results: Maximum burning rate equal or higher than reference mixture [ ]; Vigorous reaction in preliminary test [ ]; No oxidising properties [x]; Other [ ]
Method:
GLP: Yes [ ] No [ ] ?[x]
Remarks: because of chemical structure
2.12 OXIDATION: REDUCTION POTENTIAL
(Where applicable, indicate the redox potential and the conditions under which it was measured.)

Value: No data available
Method: GLP: Yes [ ] No [ ] ?[x]
Remarks:

2.13 ADDITIONAL DATA

A. Partition co-efficient between soil/sediment and water (Kd)

Value: KOC : 2.447
Method: calculated by PCKOCWIN V. 1.63
GLP: Yes [ ] No [ ] ?[x]
Remarks: very high mobility in soil.
Reference: BASF AG, department of ecology, unpublished calculation, 18, December.1998

B. Other data
(e.g. Henry's Law constant, fat solubility, surface tension (of aqueous solution), adsorption/desorption on soil, particle size distribution, etc.)
3. ENVIRONMENTAL FATE AND PATHWAYS
[Reporting of studies should give the test method, test conditions (laboratory versus field studies), test results (e.g. % degradation in specified time period) and reference. Information on breakdown products (transient and stable) should be provided when available.]

3.1 STABILITY

3.1.1 PHOTODEGRADATION
(a)
Type: Air [ ]; Water [ ]; Soil [ ]; Other [ ]
Light source: Sun light [ ]; Xenon lamp [ ]; Other [ ]
Light spectrum: nm
Relative intensity: (based on intensity of sunlight)
Spectrum of substance: (e.g. lambda (max.)> 295 nm) and epsilon[max] or epsilon [295 nm]nm
Concentration of Substance:
Temperature: °C
Direct photolysis:
Half life:
Degradation: % (weight/weight) after . . . .(exposure time)
Quantum yield: Indirect Photolysis:
Type of sensitizer:
Concentration of sensitizer
Rate constant (radical): cm³/molecule*sec
Degradation:
Method: calculated [ ]; measured[ ]
GLP: Yes [ ] No [ ] ? [ ]
Test substance: purity:
Remarks: Molecules with an adsorbance maximum of light with wavelength range of 290-600 nm electrons may get promoted from bonding orbitals to antibonding orbitals (eg. π→ π* transitions). The molecule is then in a so-called exited state. But molecules with the basic structure RSSR has an adsorption maximum near by 300 nm and a single bound. Additionally the molecule needs a chromophore group like a conjugated double bonds. Heteroatoms like oxygen makes so-called n→ n* transition are principle also possibly but commonly at longer wavelength. Due to these chemical features probably it does not seem that disodium sulphite undergoes photochemical reactions neither in air(totally soluble in water) nor in water depending on its chemical structure.
Reference:

3.1.2 STABILITY IN WATER
Type: Abiotic (hydrolysis)[ ]; biotic (sediment)[ ]
Half life: (T 1/2 : )
Degradation: at pH at °C after (exposure time)
Method:
GLP: Yes [ ] No [ ] ? [ ]
Test substance: purity:
Remarks: Disodium disulphite dissolves in water forming sodium cations, disulfite anions, and sulfur dioxide. Depending on the pH-value, sulfur dioxide, sodium hydrogen sulfite or sodium sulfite is present in aqueous solution.
Reference:
3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

a) Preferred result
Media: Air-biota[ ]; Air-biota-sediment-soil-water[ ]; Soil-biota[ ]; Water-air[ ]; Water-biota[ ]; Water-soil[ ]; Other[ ];
Method: Fugacity level I[ ]; Fugacity level II[ ]; Fugacity level III[ ]; Fugacity level IV [ ]; Other (calculation) [ ]; Other(measurement)[ ]
Results: In air %
In water %
In soil %
In sediment %
Remarks: Not relevant
Reference:

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

Results: 
Remarks: No data available
Reference:

3.5 BIODEGRADATION

Type: aerobic [ ]; anaerobic [ ]
Inoculum: adapted [ ]; non-adapted [ ];
Concentration of the chemical: related to COD [ ]; DOC [ ]; test substance [ ];
Medium: water [ ]; water-sediment [ ]; soil [ ]; sewage treatment [ ];
Degradation: % after (time)
Results: readily biodeg. [ ]; inherently biodeg. [ ]; under test condition no biodegradation observed [ ]; other [ ];
Kinetic (e.g. Zahn-Wellens-Test) % in (time)
Method: 
GLP: Yes [ ] No [ ] ? [ ]
Test substance: purity:
Remarks: Not relevant (inorganic compounds). Elimination test can not be carried out cause it is an inorganic substance. The product may lead chemical consumption of oxygen in biological sewage works or natural water. Inhibition of degradation activity in activated sludge is not to be anticipated during correct introduction of low concentrations. The substance develops sulphurdioxide in acid milieu.
Reference:

3.6 BOD5,COD OR RATIO BOD5/COD

BOD5
Method: 
Concentration: mg/L related to COD [ ]; DOC [ ]; Test substance [ ];
Value: = mg O2/L
GLP: Yes [ ] No [ ] ? [ ]
COD
Method: 
Value: = mg O2/g
GLP: Yes [ ] No [ ] ? [ ]
Ratio BOD5/COD: 
Remarks: Not relevant (inorganic compounds)
Reference:
3.7 BIOACCUMULATION

Species:
Exposure period:
Temperature:
Concentration: mg/L
BCF:
Elimination: Yes [ ] No [ ] ? [ ]
Method: (e.g. OECD, other (with the year of publication or updated of the method used))
Type of test: calculated [ ]; measured [ ]; static [ ]; semi-static [ ]; flow-through [ ]; other (e.g. field test) [ ]
GLP: Yes [ ] No [ ] ? [ ]
Test substance:
Remarks: Not expected
Reference:

3.8 ADDITIONAL REMARKS

A. Sewage treatment (information on treatability of the substance)

Results:
Remarks: No data available
Reference:

B. Other information (information that will help to focus the exposure assessment (either qualitative or quantitative))

Results:
Remarks: No data available
Reference:
4. **ECOTOXICITY**

4.1 **ACUTE/PROLONGED TOXICITY TO FISH**

(a) Type of test: static [x]; semistatic [ ]; flow-through [ ]; other [ ];
    open-system[ ]; closed system[ ]
Species: *Oryzias latipes*
Exposure period: 96 hr
Results: LC50 (96 hr) > 100 mg/L
Analytical monitoring: Yes [ ] No[x] ? [ ]
Method: OECD TG 203
GLP: Yes[x] No[ ] ? [ ]
Test substance: 98.3 %
Remarks:
Reference: Ministry of Environment (MOE), Korea (2001), The Toxicity of disodium disulphite to Fish (tested by KRICT)

(b) Type of test: static [x]; semistatic [ ]; flow-through [ ]; other [ ];
    open-system[ ]; closed system[ ]
Species: *Salmo gairdneri* (Fish, estuary, fresh water)
Exposure period: 96 hr
Results: LC50(96 hr) > 147 and < 215 mg/L
Analytical monitoring: Yes [ ] No[x] ? [ ]
Method: other : German Industrial Standard Guideline Number, DIN 38412 Group L, Part 1 and 15; 1979
GLP: Yes[x] No[ ] ? [ ]
Test substance: approx. 98 %, BASF AG No 80/339
Remarks:

4.2 **ACUTE TOXICITY TO AQUATIC INVERTEBRATES**

A. **Daphnia**

Type of test: static [x]; semistatic [ ]; flow-through [ ]; other [ ];
    open-system[ ]; closed-system[ ]
Species: *Daphnia magna*
Exposure period: 48 hr
Results: EC0 (48 hr) = 62.5 mg/L
EC50 (48 hr) = 88.76 mg/L
EC100 (48 hr) = 125.0 mg/L
Analytical monitoring: Yes [ ] No[x] ? [x]
Method: Other: EEG guideline 79/831/EWG, appendix V, part of C "Acute toxicity for Daphnia"
GLP: Yes[ ] No[x] ? [ ]
Test substance: purity > 98 % (w/w), BASF Sulphite-factory RCA B 306
Remarks:

B. **Other aquatic organisms**

No data available.

4.3 **TOXICITY TO AQUATIC PLANTS (e.g. algae)**

Species: *Scenedesmus subspicatus* (Algae)
End point: Biomass [x]; Growth rate [ ]; Other [ ]
Exposure period: 72 hr, 96 hr
Results:

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>EC20 (72 hr)</th>
<th>EC50 (72 hr)</th>
<th>EC90 (72 hr)</th>
<th>EC20 (96 hr)</th>
<th>EC50 (96 hr)</th>
<th>EC90 (96 hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biomass</td>
<td>39.2 mg/mL</td>
<td>48.1 mg/mL</td>
<td>60.0 mg/mL</td>
<td>20.0 mg/mL</td>
<td>39.8 mg/mL</td>
<td>58.0 mg/mL</td>
</tr>
</tbody>
</table>

Analytical monitoring: Yes [ ] No [ ] ? [x]
Method: other: OECD Guideline 201 “Algae, Growth Inhibition Test”
GLP: Yes [ ] No [ ] ? [x]
Test substance: purity > 98 % (w/w)
Remarks:

4.4 TOXICITY TO BACTERIA

(a) Preferred result
Type of test: Aquatic [x]; Field [ ]; Soil [ ]; Other [ ]
Species: Pseudomonas putida (Bacteria)
Exposure period: 17 hr
Results: EC10 (17 hr) = 30.8 mg/L
EC50 (17 hr) = 56.1 mg/L
EC90 (17 hr) = 115.1 mg/L
Analytical monitoring: Yes [ ] No [ ] ? [x]
Method: other: DIN 38412, part 8, Determination of inhibitory effect on the cell multiplication
GLP: Yes [ ] No [ ] ? [x]
Test substance: purity > 98 % (w/w)
Remarks:

(b)
Type of test: Aquatic [ ]; Field [ ]; Soil [ ]; Other [ ]
Species: Salmonella typhimurium, Escherichia coli, and Pseudomonas aeruginosa
Exposure period: hr
Results: EC (h) = mg/L
Analytical monitoring: Yes [ ] No [ ]
Method:
GLP: Yes [ ] No [ ] ? [x]
Test substance:
Remarks: Salmonella typhimurium 59143, Escherichia coli ES-1, and Pseudomonas aeruginosa 8602 were not viable to disodium disulphite concentration of 800, 1000, and 2000 ppm, respectively, in gelatin medium. In rehydrated bone meal, Salmonella typhimurium showed no viability in 2 out of 4 cases at 4000 ppm.

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1 CHRONIC TOXICITY TO FISH
No data available.

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Type of test: static [ ]; semistatic [x]; flow-through [ ]; other [ ]; open-system [ ]; closed-system [ ]
Species: Daphnia magna
Endpoint: Mortality [ ]; Reproduction rate [x]; other [ ]
Exposure period: 21 days
Unit: mg/L.
OECD SIDS          DISODIUM DISULPHITE

Results: NOEC > 10.0 mg/L
LC0 > 10.0 mg/L
Analytical monitoring: Yes[ ] No[x] ?[ ]
GLP: Yes[x] No[ ] ?[ ]
Test substance: purity > 98 % (w/w)

4.6 TERRESTRIAL ORGANISMS

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS
No data available.

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species: Tomato leaves
End-point: Emergence [ ]; Growth [ ]; Other [x]
Exposure period: 5 hr
Results: 
Method: 
GLP: Yes [ ] No [ ] ? [x]
Test Substances: purity
Remarks: Treatment of tomato leaves with different concentration of disodium disulphite induced degradation of green pigments and protein. Chlorophyll content was reduced by 71.15 % and protein by 42.85 % in treated leaves at a concentration of 660 µg/mL as compared with controls.

4.6.3 TOXICITY TO OTHER NON-MAMMALIAN TERRESTRIAL SPECIES
No data available.

4.7 BIOLOGICAL EFFECTS MONITORING
No data available.

4.8 BIOTRANSFORMATION AND KINETICS
No data available.

4.9 ADDITIONAL REMARKS
No data available.
5. **TOXICITY**

5.1 **ACUTE TOXICITY**

5.1.1 **ACUTE ORAL TOXICITY**

(a) Preferred Result
Type: LD0[ ]; LD50[x] LD100[ ]; LDLo[ ]; Other [ ]
Species/strain Rat
Value: LD50= 1,540 mg/kg
Discriminating dose: 0, 800, 1250, 1600, 2000 mg/kg bw
Method: OECD TG 401
GLP: Yes[ ] No[ ] ? [x]
Test substance: Disodium disulphite-powder, purity min. 96 %, other TS
Remark: Reference: Hoechst AG (1987); unpublished studies (87.1374), 04. September. 1987

(b) Type: LD0[ ]; LD50[x] LD100[ ]; LDLo[ ]; Other [ ]
Species/strain Rat
Value: LD50= 2,480 mg/kg
Discriminating dose: unknown
Method: Not specified
GLP: Yes[ ] No[ ] ? [x]
Test substance: Disodium disulphite purity: unknown
Reference: National Technical Information Service U.S. Department of Commerce (NTIS), FDA 71-22, PB 221 825 (1972)

(c) Type: LD0[ ]; LD50[x]; LD100[ ]; LDLo[ ]; Other [ ]
Species/strain Sheep
Value: 2,515 mg/kg
Discriminating dose: N/A
Method: Yes[ ] No[ ] ? [x]

5.1.2 **ACUTE INHALATION TOXICITY**
No data available

5.1.3 **ACUTE DERMAL TOXICITY**
No data available

5.1.4 **ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION**

(a) Type: LC0[ ]; LC50[ ]; LC100[ ]; LCLo [ ]; Other [ ]
Species/strain Rat/Sherman
Route of Administration: i.m.[ ]; i.p [ ]; i.v. [x]; infusion [ ]; s.c. [ ]; Other [ ]
Exposure time: approximately 115 mg/kg bw
Value: LD0[ ]; LD50[x]; LD100[ ]; LDLo[ ]; Other [ ]
Method: Yes[ ] No[x] ?[ ]
Test substance: Disodium disulphite
5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION

(a)
Species/strain: Rabbit/Albino New Zealand
Results: Highly corrosive [ ]; corrosive [ ]; Highly irritating [ ]; Irritating [ ]; Moderate irritating [ ]; Slightly irritating [ ]; Not irritating [ ]
Classification: Highly corrosive (cause severe burns) [ ]; Corrosive (caused burns) [ ]; Irritating [ ]; Not irritating [ ]
GLP: Yes[x]. No[ ]. ?[ ]
Test substance: Disodium disulphite-powder, min. purity 96 %, Other TS
Remarks: 500 mg of the chemical was prepared into a paste with a saline solution (NaCl 0.9 %) and applied to the animal semiocclusively over a 2.5 x 2.5 cm2 area. The skin was evaluated after 30-60 min, as well as 24, 48 and 72 h after the patch was removed.
Reference: Hoechst AG (1987); unpublished studies (87.1241)
5.2.2 EYE IRRITATION/CORROSION

(a) Preferred result
Species/strain: Rabbit
Results: Highly corrosive [ ]; corrosive [ ]; Highly irritating [ ]; Irritating [x]; Moderate irritating [ ]; Slightly irritating [ ]; Not irritating [ ]
Classification: Irritating [x]; Not irritating [ ]; Risk of serious damage to eyes [ ]
Method: OECD TG 405 (1987)
GLP: Yes [x] No [ ] ? [ ]
Test substance: Disodium disulphite-powder, min. purity 96 %, other TS

5.3 SKIN SENSITIZATION

(a)
Type:
Species/strain: Guinea pig
Results: Sensitizing [ ]; Not sensitizing [x]; ambiguous [ ]
Classification: (If possible, according to EC Directive 67/548/EEC)
Sensitizing [ ]; Not sensitizing [ ]
Method: Standardized skin sensitization test
GLP: Yes [ ] No [ ] ? [x]
Test substance: 0/10 guinea pigs responded positively

5.4 REPEATED DOSE TOXICITY

(a) Preferred Result
Species/strains: Rat / Wistar
Sex: Female [ ]; Male [ ]; Male/Female [x]; No data [ ]
Route of administration: Feeding(p.o)
Exposure period: 104 weeks (F0 and F1 generations), 30 weeks (F2 generations)
Frequency of treatment: Daily
Post exposure observation period:
Dose: 0, 0.125, 0.25, 0.5, 1.0, 2.0 % in feed
Control group: Yes [x]; No [ ]; No data [ ]
Concurrent no treatment [x]; Concurrent vehicle [ ]; Historical [ ]
NOAEL: local toxicity: 0.44 % (as actual dose) or 0.5 % (in the diet)
system toxicity: 1.91 % (as actual dose) or 2 % (in the diet)
LOAEL: 0.92 % (actual dose) or 1.0 % (in the diet)
Results: The most sensitive criteria of sulphite damage in the present studies turned out to be the presence of occult blood in the faeces and changes in gastric morphology. At 0.5 % of this chemical, neither these nor any of the other criteria were affected. Taking the loss of sulphite into account, the NOAEL was 0.44 % Na2S2O5 which corresponds to an intake of 217 mg Na2S2O5 /kg b.w./day.
Method: Other (multigeneration study)
GLP: Yes [ ]; No [x]; ? [ ]
Test substance: source : Amsterdamsche Chinine Fabriek, purity : 95-99 % (as calculated from SO2 determination)
Remark: The actual doses were 0, 0.098, 0.215, 0.44, 0.92, 1.91 % (sulphit loss occurred)

(b)
Species/strains: Rat / Wistar
Sex: Female [ ]; Male [ ]; Male/Female [x]; No data [ ]
Route of administration: Feeding(p.o)
Exposure period: 8 or 12 weeks
OECD SIDS

DISODIUM DISULPHITE

Frequency of treatment: Daily
Post exposure observation period:
Dose: 4, 6 % in feed
Control group: Yes [x]; No [ ]; No data [ ]; Concurrent no treatment [x]; Concurrent vehicle [ ]; Historical [ ]

NOEL: LOEL: Results: Feeding sulfite induce hyperplastic fundic glands and dilated glands.
Method: Subchronic study
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: Remark: The animals were fed on thiamine-supplemented feed, which was mixed with 4 or 6 % test substance

Species/strains: Rabbit
Sex: Female [ ]; Male [x]; Male/Female [ ]; No data [ ]
Route of administration: i.v.
Exposure period: 3 weeks
Frequency of treatment: 3 times/day and 5 d/weeks
Post exposure observation period:
Dose: 10, 20, 40 mg/kg
Control group: Yes [x]; No [ ]; No data [ ]; Concurrent no treatment [x]; Concurrent vehicle [ ]; Historical [ ]
NOEL: > 40 mg/kg in feed
LOEL: Results: The test was performed using 3 animals/dose (2 animals in control). During the experimental period (21 days), no dead animals were observed. Neither macroscopic nor microscopic changes were observed in the heart, lung, liver, spleen and kidney. Intravenous injection caused the formation of 2-3 cm long thrombus. The addition of 6 % parenamin (protein hydrolysate) could hinder this thrombus formation.
Method: GLP: Yes [ ]; No [ ]; ? [ ]
Test substance: Remark:

Species/strains: Pig / other: Hollaendische Landrasse
Sex: Female [ ]; Male [ ]; Male/Female [x]; No data [ ]
Route of administration: Oral feed
Exposure period: 15-19 or 48-51 weeks
Frequency of treatment: Daily
Post exposure observation period:
Dose: 0.06, 0.16, 0.35, 0.83, 1.72 % in feed
Control group: Yes [x]; No [ ]; No data [ ]; Concurrent no treatment [x]; Concurrent vehicle [ ]; Historical [ ]
NOEL: 0.35 % in feed
LOEL: Results: The testing was performed using 20 each of male and female animals for dose groups. The animals were given thiamine-supplemented feed. At 1.72 % dose, the feed intake and body weight were reduced. The mortality was not affected. The thiamine content in urine and liver was reduced dose-dependently and it was lower than control animals at 1.72-% dose. In another study 15 each of male and female animals with 1.72-% sodium metasulfite (paired feeding study), no effect on feed intake and weight gain was observed. Hematological examination showed no change in comparison with control. Besides these, no indication of blood in feces was observed. Each 14 animals of male and female were sacrificed after 15-19
weeks and the remaining animals were sacrificed after 48-51 weeks. Relative organ weight was increased in heart, kidney and spleen at 0.83 % and 1.72 % doses and in liver at 1.72 % dose. Alteration of stomach and darkening of cecum were formed at 0.83 % and 1.72 % doses. At three doses, hyperplastic in stomach mucosa was observed. Epithelial hyperplasia and neutrophilic leucocyte in the gullet was also observed. In the mucosa of blind gut at 0.83 and 1.72 % dosing, pigmented macrophage often appeared. In the highest dose, lipid-containing Kupffer’s cells were frequently observed in the liver.

GLP: [Yes ]; No [x]; ? [ ]
Test substance: source : Amsterdamsche Chinine Fabriek, purity : 95-99 %
Remarks: Standard Plate Test; Preincubations test

5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

(a) Preferred Result
Type: Bacterial reverse mutation assay
System of testing: Salmonella typhimurium TA98, TA100, 1537 & 1538
Concentration: 20 - 5000 µg/plate
Metabolic activation: With [ ]; Without [ ]; With and Without [x]; No data [ ]
Results:
Cytotoxicity conc: With metabolic activation : not observed
Without metabolic activation : not observed
Precipitation conc: + ? -
Genotoxic effects: With metabolic activation : [ ] [ ] [x]
                        Without metabolic activation : [ ] [ ] [x]
Method: OECD TG 471 (1983)
GLP: Yes [ ]; No [x]; ? [ ]
Test substance: Source : BASF Aktiengesellschaft Purity : 98 %
Remarks:
Reference: BASF AG, Dept. Toxicology, unpublished result (89/380), 09.October.1989

(b)
Type: Bacterial reverse mutation assay
System of testing: Salmonella typhimurium TA98, TA100, 1535, 1537 & 1538
Escherichia coli WP 2 (uvrA)
Concentration: 0.3 – 10000.0 µg/plate
Metabolic activation: With [ ]; Without [ ]; With and Without [x]; No data [ ]
Results:
Cytotoxicity conc: With metabolic activation : 333.3 µg/plate
                        Without metabolic activation : 10000µg/plate
Precipitation conc: + ? -
Genotoxic effects: With metabolic activation : [ ] [ ] [x]
                        Without metabolic activation : [ ] [ ] [x]
Method: Other
GLP: Yes [ ]; No [ ]; ?[x]
Test substance: Source : Baker Chemical Co., Phillipsburg
Remarks:
Reference: Microbial Mutagenesis Testing of Substances : Compound Report F76-004 Sodium Meta-Bisulfite, PB 89-193684 (1978)

(c) Type: Bacterial reverse mutation assay  
System of testing: *Salmonella typhimurium* TA1530  
Concentration: Not specified  
Metabolic activation: With [ ]; Without [x]; With and Without [ ]; No data [ ]  
Results:  
- Cytotoxicity conc: With metabolic activation: mg/plate  
  Without metabolic activation: no data  
- Precipitation conc: + ? -  
- Genotoxic effects:  
  - With metabolic activation: [ ] [ ] [ ]  
  - Without metabolic activation: [ ] [ ] [x]  
Method: Other (Ames 1975)  
GLP: Yes [ ]; No [ ]; ? [x]  
Test substance:  
Remarks:  

(d) Type: Bacterial reverse mutation assay  
System of testing: *Salmonella typhimurium* TA 92, 94, 98, 100, 1535 & 1537  
Concentration: maximum dose 50 mg/plate  
Metabolic activation: With [ ]; Without [ ]; With and Without [x]; No data [ ]  
Results:  
- Cytotoxicity conc: With metabolic activation: not observed  
  Without metabolic activation: not observed  
- Precipitation conc: + ? -  
- Genotoxic effects:  
  - With metabolic activation: [ ] [ ] [x]  
  - Without metabolic activation: [ ] [ ] [x]  
Method: Other (Ames 1975)  
GLP: Yes [ ]; No [ ]; ? [x]  
Test substance: Provided by Japan Food Additive Association, Purity: 95%  
Remarks:  

(e) Type: Bacterial reverse mutation assay  
System of testing: *Salmonella typhimurium* TA 1530  
Concentration: no details  
Metabolic activation: With [ ]; Without [ ]; With and Without [ ]; No data [x]  
Results: Positive  
- Cytotoxicity conc: With metabolic activation: mg/plate  
  Without metabolic activation: mg/plate  
- Precipitation conc: + ? -  
- Genotoxic effects:  
  - With metabolic activation: [ ] [ ] [ ]  
  - Without metabolic activation: [ ] [ ] [ ]  
Method:  
GLP: Yes [ ]; No [ ]; ? [x]  
Test substance: disodium disulphite  
Remarks: The article is not to explain, by which system was found the positive reaction.  
(f) Type: Bacterial reverse mutation assay
System of testing: *Salmonella typhimurium* TA 97
Concentration: Metabolic activation: With [ ]; Without [x]; With and Without [ ]; No data [ ]
Results: Cytotoxicity conc: With metabolic activation: mg/plate
Without metabolic activation: no data
Precipitation conc:
Genotoxic effects: + ? -
With metabolic activation: [ ] [ ] [ ]
Without metabolic activation: [x] [ ] [ ]
Method: GLP: Yes [ ]; No [ ]; ? [x]
Test substance:
Remarks: The study indicates that the mutagenic action of sodium metabisulfite depends on incubation conditions (temperature, pH, content of mannitol, ethanol etc.)

(g) Type: Bacterial reverse mutation assay
System of testing: *Escherichia coli* AP 16, AP 18
Concentration: Metabolic activation: With [ ]; Without [x]; With and Without [ ]; No data [ ]
Results: Cytotoxicity conc: With metabolic activation: mg/plate
Without metabolic activation: no data
Precipitation conc:
Genotoxic effects: + ? -
With metabolic activation: [ ] [ ] [ ]
Without metabolic activation: [x] [ ] [ ]
Method: GLP: Yes [ ]; No [ ]; ? [ ]
Test substance:
Remarks:

(h) Type: Bacterial reverse mutation assay
System of testing: *Salmonella typhimurium* G 46, C 207, 3076, TA 98, 100, 1535, 1537
Concentration: Metabolic activation: With [ ]; Without [ ]; With and Without [x]; No data [ ]
Results: Cytotoxicity conc: With metabolic activation: no data
Without metabolic activation: no data
Precipitation conc:
Genotoxic effects: + ? -
With metabolic activation: [x] [ ] [ ]
Without metabolic activation: [ ] [ ] [x]
Method: GLP: Yes [ ]; No [x]; ? [ ]
Test substance: Source: E. Mereck, Darmstadt
Remarks: Spot test

(i) Type: Bacterial reverse mutation assay
System of testing: *Salmonella typhimurium* G 46: TA 92, 1535, 100, SB 2802, 2061(his G46)
TR 3243: TA 88, 110, 90, 97(his D6610)
Concentration: 0.01-0.64 M/plate
Metabolic activation: With [ ]; Without [x]; With and Without [ ]; No data [ ]
Results:
Cytotoxicity conc: With metabolic activation : mg/plate
Without metabolic activation : 0.32 M
Precipitation conc: + ? -
Genotoxic effects:
With metabolic activation : [ ] [ ] [ ]
Without metabolic activation : [x] [ ] [ ]
Method:
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: Source : Sigma Chemical Co.
Remarks: Sodium metabisulfite showed a weak mutagenicity in the above system. These systems are characterized by mutation in his G46 or D6610. No mutagenicity was observed in other systems.

Type: Bacterial reverse mutation assay
System of testing: Salmonella typhimurium G 46 : TA 92, 1950, 2410, GW 19, TS 24
Concentration: 0, 0.1, 0.5, 1.0, 1.5, 2.0 M
Metabolic activation: With [ ]; Without [x]; With and Without [ ]; No data [ ]
Results:
Cytotoxicity conc: With metabolic activation : mg/plate
Without metabolic activation : not specified
Precipitation conc: + ? -
Genotoxic effects:
With metabolic activation : [ ] [ ] [ ]
Without metabolic activation : [x] [ ] [ ]
Method:
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: Source : Fisher Scientific Co. mixture of disodium disulphite and sodium metabisulfite
Remarks:

Type: Host mediated assay
System of testing: Salmonella typhimurium G 46, TA 1530/ Mouse
Concentration: 5 %(w/v)
Metabolic activation: With [ ]; Without [ ]; With and Without [ ]; No data [ ]
Results:
Cytotoxicity conc: With metabolic activation : mg/plate
Without metabolic activation : mg/plate
Precipitation conc: + ? -
Genotoxic effects:
With metabolic activation : [ ] [ ] [x]
Without metabolic activation : [ ] [ ] [ ]
Method:
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: Remarks:
B. NON-BACTERIAL TEST

(a) Preferred Results
Type: Cytogenetic assay
System of testing: CHL-cell
Concentration: up to 0.125 mg/mL
Metabolic activation: With [ ]; Without [x]; With and Without [ ]; No data [ ]
Results:
Cytotoxicity conc:
With metabolic activation: mg/plate
Without metabolic activation: not observed
Precipitation conc:
Genotoxic effects: + ? -
With metabolic activation: [ ] [ ] [ ]
Without metabolic activation: [ ] [ ] [x]
Method:
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: Source : Japan Food Additive Association, Purity : 95 %
Remarks:

(b) Type: Cytogenetic assay
System of testing: Embryonic lung cell WI-38
Concentration: 2.5, 25, 250 µg/mL
Metabolic activation: With [ ]; Without [x]; With and Without [ ]; No data [ ]
Results:
Cytotoxicity conc:
With metabolic activation: mg/plate
Without metabolic activation: mg/plate
Precipitation conc:
Genotoxic effects: + ? -
With metabolic activation: [ ] [ ] [ ]
Without metabolic activation: [x] [ ] [ ]
Method:
GLP: Yes [ ]; No [ ]; ? [x]
Test substance:
Remarks: Test substance indicates the inhibition of cell division and remarkable damage (aberration) in anaphase cells.

(c) Type: Cytogenetic assay
System of testing: Human embryonic lung cell WI-38
Concentration: mg/plate
Metabolic activation: With [ ]; Without [x]; With and Without [ ]; No data [ ]
Results:
Cytotoxicity conc:
With metabolic activation: mg/plate
Without metabolic activation: mg/plate
Precipitation conc:
Genotoxic effects: + ? -
With metabolic activation: [ ] [ ] [ ]
Without metabolic activation: [x] [ ] [ ]
Method:
GLP: Yes [ ]; No [ ]; ? [x]
Test substance:
Remarks: The result showed non-correlation with other testing systems. No detailed experimental information.
**5.6 GENETIC TOXICITY IN VIVO**

(a) Preferred Result

Type: Cytogenetic assay  
Species/Strains: Rat/Albino  
Sex: Female [ ]; Male [x ]; Male/Female [ ]; No data [ ]  
Route of Administration: Oral  
Exposure period: Max. 5 days  
Doses: 0, 30, 700, 1200 mg/kg  
Results: Negative  
Method: chromosome aberration test  
GLP: Yes [ ]; No [ ]; ? [x]  
Test substance: Provided by FDA US, no detail information  
Remarks: No adverse effect on bone marrow cells.  

(b) Type: Cytogenetic assay
Species/Strains: Chinese Hamster, Mouse
Sex: Female [ ]; Male [ ]; Male/Female [x]; No data [ ]
Route of Administration: Gavage
Exposure period: 2 times applications
Doses: Equivalent to 660 mg/kg (normal animal), 330 mg/kg (deficient animal) SO2
Results: Negative
Method: Other
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: Disodium disulphite
Remarks: The study was performed using sulfite-oxidase deficient and normal animals. Sulfite-oxidase deficiency was obtained by molybdenum-deficient diet and tungsten supply. As a protein control, animals treated with cyclophosphamid were used.

(c) Type: Rodent dominant lethal assay
Species/Strains: Rat/Sprague-Dawley
Sex: Female [ ]; Male [x]; Male/Female [ ]; No data [ ]
Route of Administration: Oral feed
Exposure period: 10 weeks
Doses: 0, 125, 417, 1250 mg/kg daily
Results: Negative
Method: The positive control was triethylenemelamine 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 and 20 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 d of cohabitation. To investigate the dominant lethal effect the following were investigated: total implants, total dead implants, total live implants, preimplantation loss. Total corpora lutea were also recorded.
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: source : J.T. Baker Chemical Co.
Remarks:
Reference: National Technical Information Service U.S. Department of Commerce (NTIS), Study of the Mutagenic Effect of Sodium Meta-Bisulfite (76-73) by Dominant Lethal Test in Rats, PB-299 836 (1979)

(d) Type: Dominant lethal assay
Species/Strains: Rat
Sex: Female [ ]; Male [x]; Male/Female [ ]; No data [ ]
Route of Administration: Oral
Exposure period: single dose
Doses: 30, 700, 1200 mg/kg (single dose)
Results: Negative
Method: other
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: Disodium disulphite
Remarks: No adverse effect
Type: Micronucleus assay  
Species/Strains: Hamster, Mouse  
Sex: Female [ ]; Male [ ]; Male/Female [x]; No data [ ]  
Route of Administration: Gavage  
Exposure period: flushing out of bone marrow cell 30 and 6 hour after 2 times application  
Doses: Equivalent to 660 mg/kg (normal animal), 330 mg/kg (deficient animal) SO2  
Results: Negative  
Method: Other (Schimd 1973)  
GLP: Yes [ ]; No [ ]; ? [x]  
Test substance: Disodium disulphite  
Remarks: The study was undertaken using sulfite-oxidized deficient and normal animals.  
Sulfite-oxidase deficiency was obtained by molybdenum-deficient diet and tungsten supply. As a protein control, animals treated with cyclophosphamid were used.  

Type: Sister chromatid exchange assay  
Species/Strains: Hamster, Mouse  
Sex: Female [ ]; Male [ ]; Male/Female [x]; No data [ ]  
Route of Administration: s.c.  
Exposure period: animals killed 30 and 6 hour after 2 equal dose  
Doses: Equivalent to 50 mg/kg, 660 mg/kg (normal animal), 165 mg SO2/kg (enzyme deficient animal) calculated as SO2  
Results: Negative  
Method: other (Schwarzacher & Wolf, 1974)  
GLP: Yes [ ]; No [ ]; ? [x]  
Test substance: Disodium disulphite  
Remarks: The study was undertaken using sulfite-oxidase deficient and normal animals.  
Sulfite-oxidase deficiency was obtained by molybdenum-deficient diet and tungsten supply. As a protein control, animals treated with cyclophosphamid were used.  

5.7 CARCINOGENECITY  
(a) Preferred Result  
Species/Strains: Rat / Wistar  
Sex: Female [ ]; Male [ ]; Male/Female [x]; No data [ ]  
Route of Administration: p.o.  
Exposure period: 104 weeks  
Frequency of treatment:  
Postexposure observation period:  
Doses: 0; 0.125; 0.25; 0.5; 1; 2 % in diet  
Control group: Yes [x]; No [ ]; No data [ ];  
Concurrent no treatment [x]; Concurrent vehicle [ ]; Historical [ ]  
Results: Negative  
Method:  
GLP: Yes [ ]; No [x]; ? [ ]  
Test substance: source : Amsterdamsche Chinine Fabriek, purity : 95-99 %  
Remarks: multiple generation study referred 5.4, 5.8  
Regarding neoplastic findings, the number of lymphoreticular pulmonary tumors in males decreased with increasing levels of sulphite. The incidence of thyroid and pituitary tumors 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.  
b) Species/Strains: Rat
Sex: Female [ ]; Male [ ]; Male/Female [ ]; No data [x]
Route of Administration: Drinking water
Exposure period: about 3 years
Frequency of treatment: Daily
Postexposure observation period:
Doses: Equivalent to 350, 750 ppm as SO2
Control group: Yes [x]; No [ ]; No data [ ];
Concurrent no treatment [x]; Concurrent vehicle [ ]; Historical [ ]
Results: The study was undertaken for 2.5 years and 3 generations per dose group were used 13-19 animals. Effect of feed and water intake on the feces excretion, reproduction, lactation or incidence of tumor was not observed (NOEL > 750 ppm).
Method: 3 generation study
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: Disodium disulphite
Remarks:

5.8 TOXICITY TO REPRODUCTION

(a) Preferred Result
Type: Fertility [ ]; One generation study [ ]; Two generation study [x]; Other [ ]
Species/Strains: Rat / Wistar
Sex: Female [ ]; Male [ ]; Male/Female [x]; No data [ ]
Route of Administration: Oral feed
Exposure period: 104 weeks (F0, F1-generation), 30 weeks (F2-generation)
Frequency of treatment: Once a day
Premating exposure period: Male: 21 weeks     Female: 21 weeks
Duration of test: until the weaning of the F3 animals
Doses: 0.125, 0.25, 0.5, 1.0, 2.0 % in feed
Control group: Yes [x]; No [ ]; No data [ ];
Concurrent no treatment [x]; Concurrent vehicle [ ]; Historical [ ]
NOAEL parental : = 1.91 % (actual dose), 2 % (in the diet)
NOAEL F1 Offspring: = 1.91 % (actual dose), 2 % (in the diet)
NOAEL F2 Offspring: = 1.91 % (actual dose), 2 % (in the diet)
Results: No pronounced effects were observed on reproductive performance in any generation and no effects on gonads were seen histologically
Method: continuous breeding
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: source : Amsterdamsche Chinine Fabriek, Holland, purity : 95-99 %
Remarks:

(b) Type: Fertility [x]; One generation study [ ]; Two generation study [ ]; Other [x]
Species/Strains: Rat
Sex: Female [ ]; Male [ ]; Male/Female [ ]; No data [x]
Route of Administration: Drinking water
Exposure period: Lifetime
Frequency of treatment: Daily
Premating exposure period: Male: Female:
Duration of test:
Doses: Equivalent to 350, 750 ppm SO2
Control group: Yes [x]; No [ ]; No data [ ];
Concurrent no treatment [x]; Concurrent vehicle [ ]; Historical [ ]
NOEL parental :  = 750 ppm
NOEL F1 Offspring:  = 750 ppm
NOEL F2 Offspring:  = 750 ppm
Results: The study was undertaken for 2.5 years and 3 generations. Per dose group 13-19 animals were used. Effect of feed and water intake on the feces excretion, reproduction, lactation or incidence of tumor were not observed. Detailed description was not given (NOEL > 750 ppm).
Method:
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: Disodium disulphite
Remarks:

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

(a) Preferred Result
Species/strain: Rat / Wistar
Sex: Female [x]; male [ ]; Male/Female [ ]; No data [ ]
Route of administration: Gavage
Duration of the test: day 20 of gestation
Exposure period: day of 6-15 of gestation
Frequency of treatment: Daily
Doses: 0, 1, 5, 24, 110 mg/kg bw
Control group: Yes [x]; No [ ]; No data [ ]; Concurrent no treatment [x]; Concurrent vehicle [ ]; Historical [ ]
NOAEL Maternal Toxicity : 110 mg/kg bw/day
NOAEL Teratogenicity: 110 mg/kg bw/day
Results: Test substance did not cause any effect in implantation or survival rate in maternal and fetus. In comparison with control, no significant change was observed in the number of anomaly in soft and skeletal tissues.
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: disodium disulphite (FDA 71-22)
Remarks:
Reference: National Technical Information Service U.S. Department of Commerce (NTIS), Teratologic Evaluation of FDA 71-22 (Sodium Meta-Bisulfite), PB-221 795 (1972)

(b) Species/strain: Rabbit/Dutch
Sex: Female [x]; male [ ]; Male/Female [ ]; No data [ ]
Route of administration: Gavage
Duration of the test: day 29 of gestation
Exposure period: 6th - 18th pregrated days
Frequency of treatment: Daily
Doses: 0, 1.23, 5.71, 26.5, 123 mg/kg bw
Control group: Yes [x]; No [ ]; No data [ ]; Concurrent no treatment [ ]; Concurrent vehicle [x]; Historical [ ]
NOAEL Maternal Toxicity: 123 mg/kg bw/day
NOAEL Teratogenicity: 123 mg/kg bw/day
Results: No clear effect on nidation, or on maternal or fetal survival. In comparison with control, no change was observed in the number of anomaly in soft and skeletal tissues.
GLP: Yes [ ]; No [ ]; ? [x]
Test substance: disodium disulphite (FDA 71-22)
Remarks:
**Species/strain:** Hamster  
**Sex:** Female [ ]; male [ ]; Male/Female [ ]; No data [ ]  
**Route of administration:** Gavage  
**Duration of the test:** no details  
**Exposure period:** 6th -10th pregnant days  
**Frequency of treatment:** Daily  
**Doses:** 0, 1, 6, 26, 120 mg/kg  
**Control group:** Yes [ ]; No [ ]; No data [ ]; Concurrent no treatment [ ]; Concurrent vehicle [ ]; Historical [ ]  
**NOEL Maternal Toxicity:** 120 mg/kg bw/day  
**NOEL Teratogenicity:** 120 mg/kg bw/day  
**Results:** Test substance did not cause any effect in implantation or survival rate in maternal and fetus. In comparison with control, no change was observed in the number of anomaly in soft and skeletal tissues.  
**GLP:** Yes [ ]; No [ ]; ?[x]  
**Test substance:** Disodium disulphite  
**Remarks:**


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**Species/strain:** Rat / Wistar  
**Sex:** Female [ ]; male [ ]; Male/Female [ ]; No data [ ]  
**Route of administration:** Drinking water  
**Duration of the test:** 3 weeks before mating to 20th pregnant day  
**Exposure period:** 3 weeks before mating to 20th pregnant day  
**Frequency of treatment:** Daily  
**Doses:** 4750, 9500 mg/L (25, 50 mM)  
**Control group:** Yes [ ]; No [ ]; No data [ ]; Concurrent no treatment [ ]; Concurrent vehicle [ ]; Historical [ ]  
**NOEL Maternal Toxicity:**  
**NOEL Teratogenicity:**  
**Results:** Tested with normal and tungsten - treated animals. The tungsten brought about sulfite-oxidized deficiency. It could not identify any adverse effect induced by disodium disulphite in reproduction or teratogenicity.  
**GLP:** Yes [ ]; No [ ]; ?[x]  
**Test substance:** Disodium disulphite  
**Remarks:**


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**5.10 OTHER RELEVANT INFORMATION**

**A. Specific toxicities**

**Type:** Sensory irritation  
**Results:** Sodium metabisulfite aerosol actively evoked sensory irritation to upper respiratory tract in mice, due to presence of bisulfite anion formed in slightly alkaline pH of nasal mucosa.  
**Remarks:**  

**B. Toxicodynamics, toxicokinetics**

**Type:** Metabolism  
**Results:**  
**Remarks:** The literature states that a rapid and quantitative elimination of disodium disulphite
as sulfate was observed in man and dog.


(b) Type: Metabolism
Results: The study describes comparative metabolic examinations of injected sulfite in rats, rabbits and monkeys for the purpose of estimating the in vivo function of sulfite oxidase. The excretion rate was 1: 0.34: 0.2 in rats, rabbits and monkeys, respectively. If it is assumed that man clears sulfite similarly to the rhesus monkey, it would appear that the rat is not a good model for prediction of human toxicity.


5.11 EXPERIENCE WITH HUMAN EXPOSURE

(a) Type: Respiratory disease
Results: Four cases of respiratory diseases probably due to the exposure or handling of sulfur derivates were presented. The responsibility of theses compounds stands on the clinical history, biological cellular tests and for one of them on the evolution under a metabisulfite-free diet and a positive oral provocation test at 5 mg.


(b) Type: Asthma
Results: 6 or 20 presented a positive reaction, confirmed in 4 of 20 by double-blind challenge.

Remarks: Oral challenge tests were carried out with sodium metabisulfite solution doses of 5, 10, 25, 50 and 100 mg in 20 children aged 7-14 years with steroid-dependent bronchial asthma.


(c) Type: Life-threatening asthma
Results: Sodium metabisulfite in food and drugs provoked life-threatening asthma. In one case, a 67-yr-old woman developed severe asthma almost immediately after ingesting a salad with a vinegar based dressing (the vinegar contained sodium metabisulfite). During oral challenge studies 2 weeks later, she developed severe bronchospasm within 30 min of ingesting sodium metabisulfite. In another case, a 23- yr-old woman developed rapid deterioration of moderately severe asthma following administration of an infusion of dexamethasone (24 mg) and an injection of metoclopramide (metoclopramide) (10 mg); both drugs contained sodium metabisulfite. Challenge reactions to sodium metabisulfite were positive. Orally administered dexamethasome which did not contain sodium metabisulfite induced no bronchospasm. The patient improved significantly during 6 months on a sodium metabisulfite free diet. It was suggested that the use of sodium metabisulfite as a preservative and anti-oxidant may need re-evaluation.


(d) Type: Dermal disease
Results: acute urticaria attack.
Remarks: Case report of a 47-year-old man with severe acute intermittent urticaria. A placebo-controlled oral challenge test with 50 mg sodium disulfite

(e) Type: Patch-test
Results: positive
Remarks: Case report of contact dermatitis and asthma from sodium metabisulfite in a photographic technician. Patch-test with sodium metabisulfite 5 % pet.
Reference: Jacobs M C, R.J.G. Rycroft. Contact dermatitis and asthma from sodium metabisulfite in a photographic technician. Contact Dermatitis. 33, 65-66, 1992

(f) Type: Patch-test
Results: positive
Remarks: Case report of a 39-year old man with dermatitis. Patch-test with sodium metabisulfite 2, 5, and 10 % in water. Control tests at 10 % in 5 subjects were all negative.

(g) Type: Occupational asthma
Results: Two cases of occupational asthma in laundry workers exposed to sodium metabisulfite have been reported.

(h) Type: Patch-test
Results: negative
Remarks: Patch-tests in five patients with ocular hypersensitivity to eyes-drops also among other compounds.

(i) Type: Patch-test
Results: positive
Remarks: A thirty-year old male with erythematous vesiculapular skin eruptions with extreme pruritus on both hands showed positive patch-test reaction to DSD (10, 20, and 50 mg in pet.). Three controls were negative. Single oral provocation test with DS (5, 30, 50, and 100 mg in citric acid) gave neither skin nor pulmonary manifestations.

(j) Type: Patch-test
Results: positive
Remarks: A 31-year-old woman with psoriasis developed acute allergic contact dermatitis during topical drug trial. Patch testing with ingredients showed a positive reaction to DSD (1 and 0.2 % in pet.).
Reference: Vestergaard LL., K. E Andersen. Am. J. Contact Dermatitis. 6, 174-175, 1995

(k) Type: Anaphylaxis
Results: A case of metabisulfite induced anaphylaxis is presented in which convincing evidence of an IgE-mediated mechanism of action was found. The patient demonstrated urticaria, angioedema, nasal congestion, and apparent nasal polyp swelling following provocative challenge with sodium metabisulfite. Skin test to metabisulfite was positive as was a basophil histamine release test when the
patient's cells were incubated with metabisulfite. A review of metabisulfite induced allergic reactions in which an IgE-mediated mechanism demonstrated is presented

Remarks:

(1)
Type: Bronchospasm
Results: A case is reported of a patient with episodes of bronchospasm requiring hospital admission after handling disodium disulphite on the job. Skin tests for sodium metasulfite at a concn 10 mg/mL were negative. A simple blind oral provocation test of sodium metasulfite (1, 5, 20, and 50 mg) in acid medium was positive at the 50-mg dose, eliciting bronchial and nasal symptoms, and a decrease in CVF, FEVI, and PEF of more than 20% over baseline values. The episode of bronchospasm has not recurred in the workplace since exposure to disodium disulphite was eliminated. Oral provocation with metasulfite in acid medium is considered as a good technique for confirming the diagnosis of these cases.

Remarks:
6. REFERENCES


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1991


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Substances: Compound Report F76-004 Sodium Meta-Bisulfite, PB 89-193684,1978

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UNEP PUBLICATIONS  59


ROBUST STUDY SUMMARIES

Disodium disulphite (CAS No. 7681-57-4)
PHYSICAL/CHEMICAL ELEMENTS

1) MELTING POINT

TEST SUBSTANCE

- Identity: Disodium Disulphite (CAS NO. 7681-57-4)
- Source: BASF corporation, NR 80/339
- Purity: 95%

METHOD

- Method/guideline followed: Not stated
- GLP: No details
- Year: 1999

RESULTS

- Melting point value in °C: Not stated
- Decomposition: Yes --- 150°C
- Sublimation (yes/no/ambiguous): Not stated
  - Remarks: solid temperature 150°C (decompose to form sulfur dioxide)

CONCLUSIONS

Decomposition starts at 150°C

DATA QUALITY

- Reliabilities: Reliable with restrictions.

REFERENCES (Free Text)

BASF AG safety data sheet sodium metadisulfite, 06. January, 1999

OTHER

- Last changed: September, 2001
- Order number for sorting

⇒ Remarks
4) PARTITION COEFFICIENT

TEST SUBSTANCE

• Identity : Disodium Disulphite (CAS NO. 7681-57-4)
⇒ Remarks : Source : BASF corporation, NR 80/339
  Purity : Natriumpyrosulfit 95 %
  1-Octano : > 99 %, Merck, Water : demineralizes

METHOD

• Method/guideline followed : Not stated
• GLP : No details
• Year : 1998
⇒ Remarks : Test condition was not stated and Test chemical was analyzed by atomic absorption-spectrometric regulation.

RESULTS

• Log Pow : -3.7
• Temperature : 25ºC
⇒ Remarks :

- Measured result

<table>
<thead>
<tr>
<th>substance name</th>
<th>substance content</th>
<th>balanced distribution(Pow)</th>
<th>Log Pow</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C(octanol) X 10^-3:</td>
<td>C(water) : g/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>g/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disodium</td>
<td>2.58</td>
<td>15.1</td>
<td>1.7E10^-4</td>
</tr>
<tr>
<td>disulphite</td>
<td>6.71</td>
<td>60.3</td>
<td>1.1E10^-4</td>
</tr>
<tr>
<td></td>
<td>16.0</td>
<td>30.1</td>
<td>5.3E10^-4</td>
</tr>
<tr>
<td>Mean value</td>
<td></td>
<td>2.2E10^-7</td>
<td>-3.7 ±0.3</td>
</tr>
</tbody>
</table>

a) Pow = C (octanol) / C (water)
C : concentration of the substance in 1-octanol or water

CONCLUSIONS

• Log Pow : -3.7.
⇒ Remarks

DATA QUALITY

• Reliabilities : Reliable with restrictions.
⇒ Remarks :

REFERENCES (Free Text)


OTHER

• Last changed : September, 2001
• Order number for sorting
⇒ Remarks
5) WATER SOLUBILITY

TEST SUBSTANCE

- Identity: Disodium Diisulphite (CAS NO. 7681-57-4)
  ⇒ Remarks

METHOD

- Method/guideline followed: Not stated
- GLP: No details
- Year: 1999
  ⇒ Remarks:

RESULTS

- Value (g/L) at Temperature: 470 g/L at 20°C
- Description of solubility: high soluble
- pH value and concentration at Temperature: Not stated
- *pKa value at 25°C: Not stated.
  ⇒ Remarks:

CONCLUSIONS

- Solubility in water: 470 g/L at 20°C
  ⇒ Remarks: This chemical is high soluble in water with 20°C.

DATA QUALITY

- Reliabilities: Reliable with restrictions.
  ⇒ Remarks:

REFERENCES (Free Text)

- BASF AG, Sicherheitsdatenblatt Natriumdisulfit, 30. October. 2000

OTHER

- Last changed: September. 2001
- Order number for sorting
  ⇒ Remarks
**TEST SUBSTANCE**

- Identity: Disodium Disulphite (CAS NO. 7681-57-4)
- Remarks: Source: disodium disulphite, 98.3%

**METHOD**

- Method / guideline followed: OECD TG 203
- Type (test type): static
- GLP: Yes
- Year: 2001 (study performed)
- Species / Strain / Supplier: *Oryzias latipes* (Medaka)
- Analytical monitoring: No
- Exposure period: 96 hours
- Statistical methods: Not relevant (limit test)
- Remarks
  - Test fish
    - Age: 9 months
    - Body length: 3.2 ±0.1 cm
    - Body weight: 0.25 ±0.02 g
  - Test condition:
    - Details of test: static
    - Dilution water source: underground water by passing through activated carbon and the membrane filter (1µm)
    - Dilution water chemistry: not stated
    - Stock and test solution and how they are prepared: dilution water was used to prepare the stock solution
    - Concentrations dosing rate, flow-through rate, in what medium: control, 100 mg/L
    - Vehicle/solvent and concentrations: not used
    - Stability of the test chemicals solutions: not stated
    - Exposure vessel type: 5 L glass aquarium non-sealed (25 x 14 x 25 cm), light/dark=16/8 hr
    - Number of replicates, fish per replicate: no replicates, 7 fish per concentration
    - Water chemistry in test (O2, pH) in the control and one concentration where effects were observed: DO 4.8 - 8.6; pH: 6.25 - 7.39
  - Test temperature range: 23.9 - 24.5ºC
  - Methods of calculating mean measured concentration: not relevant (limit test)

**RESULTS**

- Nominal concentration (as mg/L): 100.0
- Measured concentration (as mg/L): not stated
- Unit (results expressed in what unit): mg/L
- Statistical results as appropriate: not relevant
- Element value:
  - 96 hr - LC50 > 100 mg/L
- Remarks
  - Biological observations:
    - Observable symptoms of intoxication: All normal
  - Table showing cumulative mortality: no death was observed

<table>
<thead>
<tr>
<th>Nominal conc. (mg/L)</th>
<th>Number of fish at the beginning</th>
<th>Cumulative number of dead fish</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>24 hr</td>
</tr>
<tr>
<td>0.0</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>100.0</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Nominal conc. (mg/L)</td>
<td>Number of fish at the beginning</td>
<td>Cumulative number of dead fish</td>
</tr>
<tr>
<td>----------------------</td>
<td>---------------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24 hr</td>
</tr>
<tr>
<td>0.0</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>100.0</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Nominal conc. (mg/L)</td>
<td>Number of fish at the beginning</td>
<td>Cumulative number of dead fish</td>
</tr>
<tr>
<td>---------------------</td>
<td>---------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td></td>
<td>24 hr</td>
<td>48 hr</td>
</tr>
<tr>
<td>0.0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>100.0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
10-2) ACUTE TOXICITY TO FISH

TEST SUBSTANCE

- Identity: Disodium Disulphite (CAS NO. 7681-57-4)
  ⇒ Remarks: Source: disodium disulphite, approx. 98 %, (B ASF AG No 80/339)

METHOD

- Method / guideline followed: (other) German Industrial Standard Guideline Number DIN 38412 Group L, part 1 and part 15
- Type (test type): static
- GLP: No
- Year: 1979
- Species / Strain / Supplier: rainbow trout (Salmo gairdneri), Obtained from Forellenhof fredelsloh 3413 morin towards 1, FRG.
- Analytical monitoring: No
- Exposure period: 96 hours
- Statistical methods: Probit Analysis
  ⇒ Remarks

  - Test fish
    - Body length: 7.6 cm (avg.)
    - Body weight: 5.4 g (avg.)
    - Duration of adaptation: 3 days

  - Test condition:
    - Details of test: static
    - Dilution water source: tap water
    - Dilution water chemistry: reconstituted freshwater was prepared from demineralized tap water that was resalted by the addition of 344 mg/L CaSO₄·2H₂O, 124 mg/L MgSO₄·7H₂O, 70 mg/L NaHCO₃ and 3 mg/L KCl, Oxygen content: > 6 mg/L, pH: 7 - 8
    - Stock and test solution and how they are prepared: not stated
    - Concentrations dosing rate, flow-through rate, in what medium: 0, 68.1, 100.0, 147.0, 215.0, 316.0 mg/L were tested
    - Vehicle/solvent and concentrations: not stated
    - Stability of the test chemicals solutions: not stated
    - Exposure vessel type: All-glass aquarium non-sealed (30 x 22 x 24 cm)
    - Number of replicates, fish per replicate: 10 fish per concentration
    - Water chemistry in test (O₂, pH) in the control and one concentration where effects were observed: Oxygen content: > 6 mg/L, pH: 7 - 8

  pH values during the test

<table>
<thead>
<tr>
<th>Conc. mg/L</th>
<th>Starting pH</th>
<th>Ending pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>7.6</td>
<td>7.4</td>
</tr>
<tr>
<td>68.1</td>
<td>6.5</td>
<td>7.1</td>
</tr>
<tr>
<td>100.0</td>
<td>6.1</td>
<td>6.8</td>
</tr>
<tr>
<td>147.0</td>
<td>6.0</td>
<td>5.0</td>
</tr>
<tr>
<td>215.0</td>
<td>5.6</td>
<td>4.3</td>
</tr>
<tr>
<td>316.0</td>
<td>5.0</td>
<td>2.7</td>
</tr>
<tr>
<td>Conc. mg/L</td>
<td>Starting pH</td>
<td>Ending pH</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------</td>
<td>-----------</td>
</tr>
<tr>
<td>0.0</td>
<td>7.6</td>
<td>7.4</td>
</tr>
<tr>
<td>68.1</td>
<td>6.5</td>
<td>7.1</td>
</tr>
<tr>
<td>100.0</td>
<td>6.1</td>
<td>6.8</td>
</tr>
<tr>
<td>147.0</td>
<td>6.0</td>
<td>5.0</td>
</tr>
<tr>
<td>215.0</td>
<td>5.6</td>
<td>4.3</td>
</tr>
<tr>
<td>316.0</td>
<td>5.0</td>
<td>2.7</td>
</tr>
<tr>
<td>Conc. mg/L</td>
<td>Starting pH</td>
<td>Ending pH</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------</td>
<td>-----------</td>
</tr>
<tr>
<td>0.0</td>
<td>7.6</td>
<td>7.4</td>
</tr>
<tr>
<td>68.1</td>
<td>6.5</td>
<td>7.1</td>
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<tr>
<td>100.0</td>
<td>6.1</td>
<td>6.8</td>
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<tr>
<td>147.0</td>
<td>6.0</td>
<td>5.0</td>
</tr>
<tr>
<td>215.0</td>
<td>5.6</td>
<td>4.3</td>
</tr>
<tr>
<td>316.0</td>
<td>5.0</td>
<td>2.7</td>
</tr>
</tbody>
</table>
11) TOXICITY TO AQUATIC PLANTS (ALGAE)

TEST SUBSTANCE

- Identity: Disodium Disulphite (CAS No. 7681-57-4)
- Remarks: Source: disodium disulphite, > 98 % (w/w)

METHOD

- Method: OECD Guideline 201 "Algae, Growth Inhibition Test."
- Test type: static
- Element basis: area under the curve
- Exposure period: 72 hr, 96 hr
- GLP: No
- Year: 1989
- Species/Strain/Supplier: Scenedesmus subspicatus 86.81 SAG
- Analytical monitoring: No details
- Statistical methods: Not stated
- Remarks:
  - Test organism:
    - Laboratory culture: OECD- medium
    - Method of cultivation: Not stated
    - Controls:
  - Test condition:
    - Test temperature range: 20 °C
    - Growth/test medium chemistry:
    - Dilution water source:
      - Exposure vessel type: 100 mL-medium in a 250 mL -Erlenmeyer flaks
      - Water chemistry in test (pH) in at least one replicate of each concentration:

      | Conc.(mg/L) | 0 hr | 96 hr |
      |-------------|------|-------|
      | 0.0         | 8.20 | 7.90  |
      | 7.8         | 7.50 | 8.00  |
      | 15.6        | 7.27 | 7.90  |
      | 31.3        | 6.97 | 7.70  |
      | 62.5        | 6.60 | 4.80  |
      | 125.0       | 6.00 | 3.30  |
      | 250.0       | 5.40 | 2.90  |
      | 500.0       | 4.38 | 2.80  |

- Stock solutions preparation:
- Light levels and quality during exposure:
  - Test design:
    - Concentration: 7.8 – 500.0 mg/L
    - Initial cell number in cells/mL: 1 x 10^4
  - Methods of calculating mean measured concentration: Not stated

RESULTS

- Nominal Concentration in mg/L: 7.8, 15.6, 31.3, 62.5, 125.0, 250.0, 500.0 (mg/L)
(1) 72 hr
EC20 : 39.2 mg/L
EC50 : 48.1 mg/L
EC90 : 60.0 mg/L

(2) 96 hr
EC20 : 20.0 mg/L
EC50 : 39.8 mg/L
EC90 : 58.0 mg/L

- Was control response satisfactory? Yes (cell density increased 54 times after 72 hr)
- Statistical results, as appropriate

⇒ Remarks:
- Biological observations
  - cell density of each flask at each measuring point

Duration of the test : 72 hr

<table>
<thead>
<tr>
<th>Nominal Conc. (mg/L)</th>
<th>% of control</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>100.00</td>
</tr>
<tr>
<td>7.8</td>
<td>121.41</td>
</tr>
<tr>
<td>15.6</td>
<td>113.19</td>
</tr>
<tr>
<td>31.3</td>
<td>106.86</td>
</tr>
<tr>
<td>62.5</td>
<td>1.55</td>
</tr>
<tr>
<td>125.0</td>
<td>0.10</td>
</tr>
<tr>
<td>250.0</td>
<td>0.10</td>
</tr>
<tr>
<td>500.0</td>
<td>0.00</td>
</tr>
</tbody>
</table>

The EC - values are given in nominal concentration.
EC20 : 39.2 mg/L
EC50 : 48.1 mg/L
EC90 : 60.0 mg/L

Duration of the test: 96 hr

The EC - values are given in nominal concentration.
EC20 : 20 mg/L
EC50 : 39.8 mg/L
EC90 : 58 mg/L

- Growth curves

<table>
<thead>
<tr>
<th>Nominal Conc. (mg/L)</th>
<th>% of control</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>100.00</td>
</tr>
<tr>
<td>7.8</td>
<td>109.47</td>
</tr>
<tr>
<td>15.6</td>
<td>84.31</td>
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<tr>
<td>31.3</td>
<td>68.83</td>
</tr>
<tr>
<td>62.5</td>
<td>0.22</td>
</tr>
<tr>
<td>125.0</td>
<td>0.00</td>
</tr>
<tr>
<td>250.0</td>
<td>0.00</td>
</tr>
<tr>
<td>500.0</td>
<td>0.00</td>
</tr>
</tbody>
</table>

CONCLUSIONS
12) ACUTE TOXICITY TO INVERTEBRATES (DAPHNIA)

TEST SUBSTANCE

• Identity: Disodium disulphite (CAS NO. 7681-57-4)
⇒ Remarks: Source: disodium disulphite, > 98 %(w/w), (BASF sulfite - factory RCA B 306)

METHOD

• Method: EEC guideline 79/831/EWG, appendix V, part of C
• Test type: 48 hr, immobilization test
• GLP: No
• Year: 1989
• Analytical monitoring: No details
• Species/Strain/Supplier: Daphnia magna
• Test details: static
• Statistical methods: Probit Analysis
⇒ Remarks:

– Test organism:
  - Source, Supplier, any pretreatment, breeding method: The clone of Daphnia straus used was supplied by Institut National de Recherche Climique Appliquee, France, in 1978. The Daphnids are cultured under standard conditions in the laboratory for environmental analytics and ecology of the BASF AG Ludwigshafen bred.
  - Age at study initiation: 2 - 24 hrs

– Test condition:
  - Stock solution preparation: not stated
  - Test temperature range: 19 – 21 °C
  - Exposure vessel type: not stated
  - Dilution water source: not stated
  - Dilution water chemistry: hardness=2.88 [m mol/L]; Ca: Mg = approx. 4:1; alkalinity = 0.97 [m mol/L]
  - Lighting: Day: Night rhythm 16:8 hours
    - Density of light: approx. 5 Microstone/(m*m*s) in the Wavelength coverage of 400 - 750 nm
  - Water chemistry in test: Oxygen content: > 2 mg/L; pH=8.0
  - Element (unit) basis: immobilization
  - Test design (volume/animals: 2 mL, number of animals/vessel: 5, total number of animals/concentration: 20, replicates: 4)
  - Method of calculating mean measured concentrations: Not stated
  - Exposure period: 48 hr
  - Analytical monitoring: No

RESULTS

• Nominal concentration (as mg/L): 7.8, 15.6, 31.3, 62.5, 125.0, 250.0, 500.0
• Measured concentration (as mg/L): not stated
• Units (results expressed in what unit): mg/L
• EC50 (48 hrs)=88.76 mg/L, NOEC=62.5 mg/L
• Statistical results, as appropriate: not stated
⇒ Remarks:

- Biological observations
  - Number immobilized as compared to the number exposed: none
  - Concentration response with 95 % confidence limit
Duration of the test : 3 hr  
EC50 = 148.99 mg/L  
CI 95% = 82.6 - 215.38 mg/L  
EC0 = 62.5 mg/L  
EC100 = 250 mg/L  

Duration of the test : 24 hr  
EC50 = 88.76 mg/L  
CI 95% = 88.76 - 88.76 mg/L  
EC0 = 62.5 mg/L  
EC100 = 125 mg/L  

Duration of the test : 48hr  
EC50 = 88.76 mg/L  
CI 95% = 88.76 - 88.76 mg/L  
EC0 = 62.5 mg/L  
EC100 = 125 mg/L  

Cumulative immobilization

<table>
<thead>
<tr>
<th>Conc. [mg/L]</th>
<th>0 h</th>
<th>3 h</th>
<th>6 h</th>
<th>24 h</th>
<th>48 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15.6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>31.3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>62.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>125.0</td>
<td>0</td>
<td>6</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>250.0</td>
<td>0</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>500.0</td>
<td>0</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>0.0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

-Was control response satisfactory : Yes

CONCLUSIONS

For Disodium disulphite, 24 hr-EC50 value was 88.76 mg/L. Experimental designs and results were well documented and prescribed conditions in the guideline were well satisfied.
⇒ Remarks :

DATA QUALITY

• Reliabilities : Reliable with restrictions.
⇒ Remarks :

REFERENCES (Free Text)


OTHER

• Last changed : September 2001
• Order number for sorting
⇒ Remarks :
HEALTH ELEMENTS

13) ACUTE TOXICITY

TEST SUBSTANCE

- Identity: Disodium disulphite - powder (CAS No. 7681-57-4)
  ⇒ Remarks: Source: Hoechst AG, Purity: 96 % (2 % Na\textsubscript{2}SO\textsubscript{3}, 2 % Na\textsubscript{2}SO\textsubscript{4})

METHOD

- Method/guideline followed: OECD TG 401
- Type: Acute oral toxicity test
- GLP: yes
- Year (study performed): 1987
- Species/Strain: Rat / Wistar
- Sex: male and female
- No. of animals per sex per dose: 5 animals/sex/dose
- Vehicle: water
- Route of administration: oral (gavage)

REMARKS FIELD FOR TEST CONDITIONS

- Age: 7 weeks (male) and 8 weeks (female)
- Doses: 800, 1250, 1600 mg/kg (female), 1250, 1600, 2000 mg/kg (male)
- Volume administered: 10 mL/kg bw
- Concentration: 8, 12.5, 16, 20 % (w/v)
- Post dose observation period: 14 days

RESULTS

- LD\textsubscript{50} with confidence limits: 1540 (1290 - 1960, p=0.05) mg/kg bw (male/female)
  - Male: 1630 (1210 - 2260, p=0.05) mg/kg bw
  - Female: 1420 (1040 - 2110, p=0.05) mg/kg bw
- Number of deaths at each dose level:
  Males: 1/5, 2/5 and 4/5 in the 1250, 1600 and 2000 mg/kg dose groups respectively
  Females: 0/5, 1/5 and 4/5 in the 800, 1250 and 1600 mg/kg dose groups respectively

REMARKS FIELD FOR RESULTS

- Time of death

Dead animals were observed at day 1 after dosing for male and female.

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Lethality</th>
<th>Time of death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>male</td>
<td>female</td>
</tr>
<tr>
<td>800</td>
<td>-</td>
<td>0/5</td>
</tr>
<tr>
<td>1250</td>
<td>1/5</td>
<td>1/5</td>
</tr>
<tr>
<td>1600</td>
<td>2/5</td>
<td>4/5</td>
</tr>
<tr>
<td>2000</td>
<td>4/5</td>
<td>-</td>
</tr>
</tbody>
</table>

- Description, severity, time of onset and duration of clinical signs at each dose level: The symptoms observed in male and female animals were the reduction of activity, crouching, retracted flanks, ruffled fur, irregular breathing and a stiff-legged gait. Additionally, males in the 2 high dose groups displayed prone-position, contracted eyelids, and apathy. After the first day the symptoms were reversed in the surviving animals.
– Necropsy findings, included doses affected: The g.i. tract was filled with blood, the mucosa of the stomach was lightly reddened and the liver was dark in color. At the end of the experiment the surviving animals were sacrificed and were found to be free of any unusual gross abnormalities. Body weight gain was not influenced by treatment.

CONCLUSIONS

LD_{50} was calculated to be 1540 mg/kg with a 95 % confidence interval of 1290 - 1960 mg/kg bw

DATA QUALITY

- Reliabilities: Reliable without restriction

REFERENCES (Free Text)

Hoechst AG, Unpublished studies (87.1374), 04.Sept.1987

OTHER

- Last changed (administrative field for updating): September 2001
- Order number for sorting (administrative field)
**GENETIC TOXICITY ELEMENTS**

### 14) GENETIC TOXICITY IN VIVO (CHROMOSOMAL ABERRATIONS)

#### TEST SUBSTANCE

- **Identity**: Disodium disulphite (CAS No. 7681-57-4)
- **Remarks**: Provided by Food and Drug Administration, US

#### METHOD

- **Method/guideline followed**: other
- **Type (test type)**: Cytogenetic *in vivo* assay
- **GLP**: No details
- **Year (study performed)**: 1972
- **Species**: Rat
- **Strain**: Albino
- **Sex**: male
- **Route of administration**: oral
- **Doses/concentration levels**: 0, 30, 700, 1200 mg/kg
- **Exposure period**: Animals were treated either one time and then sacrificed in 6, 24 or 48 h, or they were treated once/day for 5 d, and then were sacrificed in 6 h after the last treatment.
- **Statistical methods**: Chi-square test

#### REMARKS FIELD FOR TEST CONDITIONS

- **Age at study initiation**: Unknown
- **No. of animals per dose**: 5 animals/dose/time point (3 rats used in negative control)
- **Vehicle**: Unknown
- **Duration of test**: 1 to 5 days
- **Frequency of treatment**: single & multiple (once a day for 5 day)
- **Sampling times and number of samples**: 6, 24, 48 hr subsequent to intubation or 6 hr after last intubation (subacute), 50 bone marrow cells per animal were evaluated.
- **Control groups (e.g. vehicle, positive, negative)**: The positive control was triethylenemelamine injected i.p. at a dose of 0.4 mg/kg.
- **Clinical observations performed**: not stated
- **Organs examined at necropsy**: not stated
- **Criteria for evaluating results**: Number and type of chromosomal aberrations (except gabs), mitotic index
- **Criteria for selection of M.T.D.**: LD50

#### RESULTS

- **Effect on mitotic index**: The mitotic index was reduced in the high dose groups after all single administration time points which indicates that the test substance reached the bone marrow to a sufficient level
- **Genotoxic effects**: negative
- **Statistical results, as appropriate**
OECD SIDS

DISODIUM DISULPHITE

<table>
<thead>
<tr>
<th>Dosage (mg/kg)</th>
<th>time</th>
<th>Mitotic Index(%)</th>
<th>No. of Animal</th>
<th>No. of cell</th>
<th>Cell with Breaks(%)</th>
<th>Cell with Rearrangements(%)</th>
<th>Cell with more than one type of aberr(%)</th>
<th>Cell with Aberr(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEM(0.4)</td>
<td>24</td>
<td>1.95</td>
<td>5</td>
<td>250</td>
<td>36.0</td>
<td>7.2</td>
<td>5.6</td>
<td>37.6</td>
</tr>
<tr>
<td>(-)</td>
<td>6</td>
<td>1.95</td>
<td>3</td>
<td>150</td>
<td>1.3</td>
<td>0</td>
<td>0</td>
<td>1.3</td>
</tr>
<tr>
<td>30</td>
<td>6</td>
<td>2.20</td>
<td>5</td>
<td>250</td>
<td>0.4</td>
<td>0</td>
<td>0</td>
<td>0.4</td>
</tr>
<tr>
<td>700</td>
<td>6</td>
<td>2.25</td>
<td>5</td>
<td>250</td>
<td>0.8</td>
<td>0</td>
<td>0</td>
<td>0.8</td>
</tr>
<tr>
<td>1200</td>
<td>24</td>
<td>1.90</td>
<td>5</td>
<td>250</td>
<td>1.3</td>
<td>0</td>
<td>0</td>
<td>1.3</td>
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<tr>
<td>(-)</td>
<td>30</td>
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<td>2.20</td>
<td>5</td>
<td>250</td>
<td>0.8</td>
<td>0</td>
<td>0</td>
<td>0.8</td>
</tr>
<tr>
<td>1200</td>
<td>48</td>
<td>2.20</td>
<td>3</td>
<td>150</td>
<td>0.7</td>
<td>0</td>
<td>0</td>
<td>0.7</td>
</tr>
<tr>
<td>(-)</td>
<td>30</td>
<td>1.70</td>
<td>5</td>
<td>250</td>
<td>1.6</td>
<td>0</td>
<td>0</td>
<td>1.6</td>
</tr>
<tr>
<td>700</td>
<td>48</td>
<td>1.60</td>
<td>5</td>
<td>250</td>
<td>1.2</td>
<td>0</td>
<td>0</td>
<td>1.2</td>
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<tr>
<td>1200</td>
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<td>0.4</td>
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<td>0.4</td>
</tr>
<tr>
<td>(-)</td>
<td>SA</td>
<td>1.75</td>
<td>3</td>
<td>150</td>
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<td>0</td>
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<tr>
<td>30</td>
<td>SA</td>
<td>2.35</td>
<td>5</td>
<td>250</td>
<td>0.8</td>
<td>0.4</td>
<td>0</td>
<td>1.2</td>
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<tr>
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<td>SA</td>
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<td>250</td>
<td>0.8</td>
<td>0</td>
<td>0</td>
<td>0.8</td>
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<tr>
<td>1200</td>
<td>SA</td>
<td>2.10</td>
<td>3</td>
<td>150</td>
<td>0.7</td>
<td>0</td>
<td>0</td>
<td>0.7</td>
</tr>
</tbody>
</table>

* SA : Sub acute (5 days treatments)

REMARKS FIELD FOR RESULTS

- Mortality at each dose level by sex : not stated
- Description, severity, time of onset and duration of clinical signs at each dose level : not stated
- Body weight changes by dose and sex : not stated
- Food/water consumption changes by dose and sex : not stated

CONCLUSIONS

No adverse effect on bone marrow chromosomes was observed as a result of disodium disulphite treatment.

DATA QUALITY

- Reliability : Reliable with restriction

REFERENCES (Free Text)


OTHER

- Last changed (administrative field for updating) : September 2001
- Order number for sorting (administrative field)
TEST SUBSTANCE

- Identity: Disodium disulphite (CAS No. 7681-57-4)
- Remarks: Source: BASF Aktiengesellschaft, Purity: 98%

METHOD

- Method/guideline followed: OECD TG 471
- Type: Reverse mutation assay (standard plate test & preincubation test)
- System of testing: bacterial
- GLP (Y/N): No
- Year (study performed): 1983
- Species/Strain: Salmonella typhimurium TA 1535, 1537, 98, 100
- Metabolic activation
  - Species and cell type: Sprague-Dawley rats
  - Induced or not induced: Aroclor-1254-induced
- Concentrations tested: 0, 20, 100, 500, 2500, 5000 µg/plate
- Statistical Methods: Not mentioned

REMARKS FIELD FOR TEST CONDITIONS

- Test Design
  - Number of replicates: 2
  - Number of plate: 3 plate/dose (and control)
  - Positive and negative control groups and treatment:
    - negative control: solvent control, sterility control
    - positive control: -S9 mix: 10 µg 2-aminoanthracene (dissolved in DMSO) for all strains
    - +S9 mix: 5 µg N-methyl-N’-nitro-N-nitrosoguanidine for TA 100, 1535
    - 10 µg 4-nitro-o-phenylenediamine for TA 98
    - 100 µg 9-aminoacridine chloride monohydrate for TA 1537
- Solvent: DMSO (dimethylsulfoxide)
- Description of follow up repeat study
  - 1st experiment: standard plate test with and without S-9 mix
  - 2nd experiment: preincubation test with and without S-9 mix
- Criteria for evaluating results: doubling of the spontaneous mutation rate (control), dose-response relationship, reproducibility of the results

RESULTS

- Cytotoxic concentration: No bacteriotoxic effect
- Genotoxic effects
  - With metabolic activation: negative
  - Without metabolic activation: negative
- Statistical results: Not mentioned

REMARKS FIELD FOR RESULTS
CONCLUSIONS

An increase in the number of his\(^+\) revertants was not observed both in the standard plate test and in the preincubation test either without or with S9 mix.

DATA QUALITY

- Reliabilities: Reliable without restrictions

Remarks fields of reliability

Well conducted, followed GLP-like requirement.

REFERENCES

BASF AG, Dept. of Toxicology, Unpublished study (89/380), 09.Oct.1989

OTHER

- Last changed: September 2001
- Order number for sorting (administrative field)
TEST SUBSTANCE

- Identity: disodium disulphite (CAS No. 7681-57-4)
- Remarks: Source: Sigma Chemical Co., St. Louis, MO.

METHOD

- Method/guideline followed: Other
- Type: reverse mutation assay (preincubation)
- System of testing: bacterial
- GLP (Y/N): Not details
- Year (Paper received): 1986
- Species/Strain: Salmonella typhimurium TA 92, 1535, 100, 88, 110, 90, 97, 1538, 98, SB 2802, 2061
- Metabolic activation: Not applied
- Concentrations tested: 0.01-0.64 M
- Statistical Methods: No stated

REMARKS FIELD FOR TEST CONDITIONS

- Test Design
  - Number of replicates: 3-4
  - Positive and negative control groups and treatment: Only negative control used
  - Number of metaphases analysed: Not applicable

- Solvent: 0.1 M sodium phosphate buffer
- Criteria for evaluating results: The level of toxicity seen on the nutrient plates after 24 h incubation was compared to toxicity seen in the background lawns of the mutation plates scored after 48 h incubation at 37°C

RESULTS

- Cytotoxic concentration:
  No significant effects on mutagenicity of any strains at concentration up to 0.32 M
- Genotoxic effects: slightly positive
- Statistical results: Not mentioned

REMARKS FIELD FOR RESULTS

- Mutagenic response strains: G 46, TR 3243 (only the strain carrying the his D6610 or his G46)
- Condition affecting mutagenicity: bisulfit-induced mutation appear to be the result of two different mechanisms which may be a function of the repair capacity of the strains. It suggests that the deamination of cytosine may be responsible for base pair substitution mutagenesis and the deamination of cytosine may be the result of oxidative damage rather than through the direct formation of a cytosine-bisulfite adduct because the rate of bisulfite autooxidation appears to play a role in the mutagenic process.

  - Plasmid: pKM101 slightly enhanced the level of base-pair substitutions
  - Genotype: his O1242 mutation, urvB and rfa mutations affected the mutagenicity
  - pH range: In the pH range of 4.4 - 5.6, the mutagenic response was maximized for TA97. The pH of the bisulfite solution has an effect on bisulfite mutagenesis and autooxidation. If a lower pH slows the rate of autooxidation allowing more unoxidized product to be taken up by the cell, then the enhanced
mutagenicity seen after increasing the exposure length suggests that alterations in the rate of bisulfite autooxidation should have effects on the level of mutagenicity.

- **Preincubation time**: 60 - 120 min of preincubation time increased the No. of revertants
- **Statistical results**: Not mentioned

**CONCLUSIONS**

This chemical is a weak mutagen at pH 5 and 6 in *S. typhimurium* strains carrying the *his* G46 and *his* D6610 mutations.

**DATA QUALITY**

- Reliabilities: Reliable with restrictions

**REFERENCES**

Pagano DG und Zeiger E, Conducting affecting the mutagenicity of sodium bisulfite in *Salmonella typhimurium*, Mutation Research, 179, 159-166 (1987)

**GENERAL REMARKS**

The dose levels in this study are not clear. This could make it difficult to compare to other studies.

**OTHER**

- Last changed: May 2001
- Order number for sorting (administrative field)
# 16) REPEATED DOSE TOXICITY

## TEST SUBSTANCE
- **Identity**: Disodium disulphite (CAS No. 7681-57-4)
- **Remarks**: Source: Amsterdamsche Chinine Fabriek (ACF)- purity 95~99 % (as calculated from SO2 determinations)

## METHOD
- **Method/guideline followed**: Other
- **Test type**: Long-term feeding study
- **GLP**: No
- **Year**: 1971
- **Species**: Rat
- **Strain**: Wistar
- **Route of administration**: oral (feed)
- **Duration of test**: about 2 year
- **Doses/concentration levels**: 0, 0.125, 0.25, 0.5, 1.0, 2.0 %
- **Sex**: male & female
- **Exposure period**: 104 weeks (F0 and F1 generations), 30 weeks (F2 generations)
- **Frequency of treatment**: 7 d/ week
- **Control group and treatment**: basal diet containing 0 % Na2S2O5
- **Post exposure observation period**: None
- **Statistical methods**: Student’s t test and chi-square test

## REMARKS FIELD FOR TEST CONDITIONS

<table>
<thead>
<tr>
<th>Test Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>· <strong>Age at study initiation</strong>: Newly weaned rats</td>
</tr>
<tr>
<td>· <strong>No. of animals per sex per dose</strong>: 20 animals/dose/sex</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>· <strong>Vehicle</strong>: none (stock diet containing the test substance)</td>
</tr>
<tr>
<td>· <strong>Satellite groups and reasons they were added</strong>: none</td>
</tr>
<tr>
<td>· <strong>Clinical observations performed and frequency</strong>: Changes of body weight were recorded weekly for the 1st 12wk and once every 4 wk thereafter. The food consumption of each diet group was measured at intervals during 1 wk periods. Hematological investigations were performed from control, 1, and 2 % dose groups of F0 at wk 52, 78, 100, at 52, 102 wk in the F1a generation and at wk 20 of F2 generation. At week 32, 64, and 100 all rats of the F0 and F1a generation and at wk 28 those of the F2a generations were examined for occult blood in faeces. Serum activities of glutamic-oxalacetic and glutamic-pyruvic transaminases were estimated at wk 52, 104 in the F0 generation rats. Kidney function was examined in the urine from controls, 1, and 2 % dose groups, at wk 13, 28, 52, 78 and 101 in F0, at wk 28, 52, 100 in the F1 and wk 28 in the F2. Concurrently pooled urine analysis was performed for appearance, pH, glucose, albumin, occult blood, ketones and microscopy of the sediment.</td>
</tr>
<tr>
<td>· <strong>Organs examined at necropsy (macroscopic and microscopic)</strong></td>
</tr>
<tr>
<td>Interim observation on organ weight and pathological changes.</td>
</tr>
</tbody>
</table>
| 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.

RESULTS

• NOAEL(NOEL)
  – local toxicity (presence of occult blood and changes in gastric morphology) : 0.215 % Na$_2$S$_2$O$_5$ as actual dose(72 mg SO$_2$/kg b.w. day or 106 mg Na$_2$S$_2$O$_5$ /kg b.w./day) or 0.25 % (in the diet)
  – system toxicity : 1.91 % as actual dose (942 Na$_2$S$_2$O$_5$ mg /kg b.w./day) or

• Actual dose received by dose level: The SO$_2$ determinations on the diets showed considerable losses of sulphite. Proportionally the losses of sulphite decreased with increasing dietary levels of sulphite as table shown below

<table>
<thead>
<tr>
<th>Level of Na$_2$S$_2$O$_5$ added to diet(%)</th>
<th>Loss of Na$_2$S$_2$O$_5$ after storage for 1 week at –18ºC(%)</th>
<th>Actual dose level of Na$_2$S$_2$O$_5$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.125</td>
<td>22</td>
<td>0.098</td>
</tr>
<tr>
<td>0.25</td>
<td>14</td>
<td>0.215</td>
</tr>
<tr>
<td>0.5</td>
<td>12</td>
<td>0.44</td>
</tr>
<tr>
<td>1.0</td>
<td>8</td>
<td>0.92</td>
</tr>
<tr>
<td>2.0</td>
<td>5</td>
<td>1.91</td>
</tr>
</tbody>
</table>

• Toxic response/effects by dose level
  Occult blood was present in the faeces in groups given 1 % sulphite or more. Relative weights of the kidneys were increased by the 2 % sulphite level in the F2-generation females only, but this increase was accompanied by neither functional nor histological changes. Pathological examination revealed hyperplastic changes in both the fore- and glandular stomach with level of 1 and 2 % sulphite in each of the three generation. Some slight alterations were found also with 0.5 % in the stomach of the F2-generation rats. No carcinogenic effect was shown.

REMARKS FIELD FOR RESULTS

– Body weight: There was a marginal reduction in body -weight gain in both sexes of the F1 and F2-generation given 2 % sulphite, also in females F1 given 0.125, 0.25, 0.5 % sulphite and those given 0.25, 0.5 % in the F2 generation. But there was no dose-relationship and the differences could partly be explained by the higher initial body weights of controls.

– Food consumption : There was no distinct differences in food consumption.

– Thiamine content of urine and liver : The group given 2 % sulphite showed no distinct changes in the thiamine status when compared with control rats on the stock diet without extra thiamine. This indicates that thiamine added to the sulphited diets prevented thiamine deficiency even at a dietary level of 2 % sulphite

– General condition, mortality and growth : The general condition of the rats remained good during the first 72 week in the F0-generation as well as in the two descendant generations. After this, aging symptoms developed in many rats and mortality increased rapidly in nearly all group. The survival in the sulphite groups was generally higher than in the controls, except in the case of males of the F1-generation given 2 % sulphite. No deaths occurred in the females of the same group.

– Hematological findings incidence and severity: A marginally reduced haemoglobin content, haematocrit value and erythrocyte count occurred in the F0-generation females fed on 2 % sulphite at week 52, 78 and 100, while the F1 generation males at 2 % showed an increase in leucocyte count at week 102. All haematological values for test and control animals in all successive generations were within normal ranges at all stages.

– Description, severity and duration of clinical signs
  All rats in the highest dose group showed indications of occult blood in the faeces of all generations, while this effect occurred in only 13 - 60 % of the animals on diets containing 1 % sulphite. In 10 % of the females given 0.25 % and in 10 % of the males given 0.5 % sulphite slight indications of intestinal blood loss were observed in the F0-generation rats at week 32 only.

  Occult blood in the faeces
17) TOXICITY TO REPRODUCTION

**TEST SUBSTANCE**

- **Identity:** Disodium disulphite (CAS No. 7681-57-4)
- **Remarks:** Source: Amsterdamsche Chinine Fabriek (ACF), purity 95~99% (as calculated from SO₂ determinations)

**METHOD**

- **Method/guideline followed:** Other
- **Type:** multigeneration study
- **GLP (Y/N):** No details
- **Year:** 1971
- **Species:** Rat
- **Strain:** Wistar
- **Route of administration:** oral (feed)
- **Doses/concentration levels:** 0, 0.125, 0.25, 0.5, 1.0, 2.0%
- **Sex:** male/female
- **Control group and treatment:** basal diet containing 0% Na₂S₂O₅
- **Frequency of treatment:** 7 d/week
- **Duration of test:** 2 yr
- **Premating exposure period for males and female (P and F1) as appropriate:** F₀: 21 weeks
- **Statistical methods:** Student’s t test and chi-square test

**REMARKS FIELD FOR TEST CONDITIONS**

- **Test animals**
  - **Number, age, sex per dose for P:** Newly weaned rats, 20 animals/dose/sex
  - **Number, age, sex per dose for F₁a, F₂a:** 10 animals/dose/sex selected at weaning (F₁-gen.) for produce F₂a, F₂b and 10 males, 15 females of the F₂a litters were selected for producing the next generation.

- **Test design**
  - **Vehicle:** none (stock diet containing the substance)
  - **Dosing schedules and pre and post dosing observations periods for P, F₁ and F₂:** All rats of the F₀-generation were mated within their diet group at about week 21 and half of them also at week 34. 10 animals/dose/sex from the first litters were selected at weaning (F₁-gen.) for producing F₂a, F₂b and 10 males, 15 females of the F₂a litters were selected for producing the next generation. The F₀-generation rats as well as the selected F₁a-generation rats were maintained on their diet for a period of 104 weeks. Rats of the F₁a-generation were mated at week 12 and 30 to produce the F₂a and the F₂b generations. 10 males and 15 females form the F₂a litters were mated to produce an F₃a, F₃b-generation by pairing them on week 14 and 22. These litters were discarded after weaning, and the parents were kept on their diets for about 30 weeks.

  - **Mating procedures**
    Group mating was used throughout and lasted for a period of 2 week. At day 20 after the beginning of the mating period, the females were individually housed until the litters had been weaned. Records were made of the number of pups in each litter, and of the total weight of the litter at days 1, 8 and 21. On the 1st day, the litters containing more than 8 pups were reduced to that number to equalize the stress of lactation on the dams.

  - **Clinical observations performed and frequency**
All changes of body weight were recorded weekly for the 1st 12 wk and once every 4 wk thereafter. The food consumption of each diet group was measured weekly. Hematological investigations were performed with control, 1, 2 % dose groups of F0 at wk 52, 78, 100 in F1a at 52, 102 wk and at week 20 in the F2 generation. F0-, F1a- and F2-generation were examined for occult blood in faeces at week 32, 64 and 100. Serum activities of glutamic-oxalacetic and glutamic-pyruvic transaminases were estimated at week 52, 104 in F0. Kidney function was examined for the controls, 1 and 2 % dose groups, at week 13, 28, 52, 78 and 101 in F0, at week 28, 52, 100 in the F1 and week 28 in the F2. Concurrently urine analysis was performed.

- **Organs examined at necropsy (macroscopic and microscopic)**
  - Interim observation on organ weight and pathological changes.
  - Macroscopic: 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.

- **Parameters assessed during study**
  - Female fertility, the number of young per litter, the birth weight, mortality of the young.

**RESULTS**

- **NOAEL (NOEL) and LOAEL (LOEL) for P, F1, F2 and F3**
  - **NOAEL**: 2 % in the diet (actual dose 1.91 %) which is equivalent to 942 mg of Na₂S₂O₅/kg b.w/day

- **Actual dose received by dose level**: 0, 0.098, 0.213, 0.440, 0.920, 1.91 % doses result from stock diet loss.

- **Parental data and F1 as appropriate**: No consistent differences between groups in female fertility, the number of young per litter.

- **Offspring toxicity**: No consistent differences between groups in birth weight or mortality of the young. Body weight changes were seen in the offspring (F1, F2, F3). A significant reduction in the number of F2a-generation young was observed with 0.5, 1, and 2 % sulphite. During the lactation period the body weights of the young in the 2 % group were generally lower than those of the controls and significantly decreased body weights at day 8 and 21, but there was no distinct dose-related response.

**REMARKS FIELD FOR RESULTS**

- **Fertility and offspring toxicity**: 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 the 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. This reduced body weight was probably not a true substance-related effect since it could be due to a higher initial body weight in the control groups. Furthermore, these body weight changes were within or were not dramatically different from the control values of the F1 pups. 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).
There was a marginal reduction in both sexes of the F1 and F2 generation given 2 % sulphite, 0.125, 0.25, 0.5 % sulphite in the female F1 and 0.25, 0.5 % in the F2 generation. But there was no dose relationship.

Food consumption: There was no distinct differences in food consumption.

General condition, mortality and growth: The general condition of the rats remained good during the first 72 week in the two descendant generations. After this, aging symptoms developed in many rats and mortality increased rapidly in nearly all group. The survival in the sulphite groups was generally higher than in the controls, except in the case of males of the F1 generation given 2 % sulphite. No deaths occurred in the females of the same group.

Precoital interval: not stated

Duration of gestation: not stated

Gestation index (live litters/pregnancies): no details

Changes in estrus cycles: not stated

Effects on sperm: unknown

Hematological findings incidence and severity: A marginally reduced haemoglobin content, haematocrit value and erythrocyte count occurred in the F0-generation females fed on 2 % sulphite at week 57, 78 and 100, while the F1 generation males at 2 % showed an increase in leucocyte count at week 102. All haematological values for test and control animals in all successive generations were within normal ranges at all stages.

Kidney function and enzyme activity: Phenol-red excretion, specific gravity and glutamic-oxalacetic-transaminase activity in the urine were not adversely affected by the feeding of sulphite. Urine analysis values were essentially normal. Significant (p < 0.05) decreases in serum glutamic-pyruvic-transaminase values occurred at week 104 in male rats of the F0-generation receiving 0.125 % sulphite. There were no differences in transaminase between the test and control animals of this generation activities either at week 52 or at week 104.

Number of implantations: not stated
TEST SUBSTANCE

- Identity: Disodium disulphite
  ⇒ Remarks: White crystalline material (FDA 71-22)

METHOD

- Method/guideline followed: Other
- GLP: No details
- Year: 1972
- Species: Rat
- Strain: Wistar
- Route of administration: oral (gavage)
- Doses/concentration levels: 0, 1, 5, 24, 110 mg/kg bw
- Sex: Female
- Exposure period: day of 6-15 of gestation
- Frequency of treatment: daily
- Control group and treatment: Negative control: sham treated controls
  Positive control: Aspirin 250 mg/kg bw
- Duration of test: day of 20 gestation
- Statistical methods: Not described
- Statistical methods: Not described
  - Age at study initiation: Not stated
  - Number of animals per dose per sex: Not stated
  - Vehicle: water
  - Clinical observations performed and frequency:
    - Body weights: on days 0, 6, 11, 15 and 20 of gestation
    - Appearance, behaviour and food consumption: daily
  - Mating procedures: Not stated
  - Parameters assessed during study(maternal and fetal): Average body weight, pregnancy data, skeletal abnormality, soft tissue abnormality
  - Organs examined at necropsy: The numbers of implantation site, resorptions and live/dead fetuses were recorded. Fetuses were examined for the presence of external congenital abnormality, visceral examination(1/3 of fetuses) and skeletal defect(remaining 2/3 of the fetuses)

RESULTS

- NOAEL maternal toxicity: 110 mg/kg bw/day
- NOAEL teratogenicity: 110 mg/kg bw/day
- Maternal data with dose level: No clear effect on maternal toxicity
- Fetal data with dose level: No clear effect on fetal survival

REMARKS FIELD FOR RESULTS

- Reproduction data
  The administration of the disodium disulphite to pregnant rats had no clear effect on nidation, or on maternal or fetal survival.
- **Body weight**
  No significant differences were found between treatment and negative control group.

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Sham</th>
<th>Positive</th>
<th>1.0</th>
<th>5.0</th>
<th>24.0</th>
<th>110.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total No.</td>
<td>21</td>
<td>23</td>
<td>24</td>
<td>23</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Died or Aborted(before day 20)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>To term(on day 20)</td>
<td>21</td>
<td>23</td>
<td>24</td>
<td>23</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Corpora Lutea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total No.</td>
<td>236</td>
<td>266</td>
<td>274</td>
<td>266</td>
<td>282</td>
<td>270</td>
</tr>
<tr>
<td>Average/dam mated</td>
<td>9.83</td>
<td>11.1</td>
<td>11.4</td>
<td>11.1</td>
<td>11.8</td>
<td>11.3</td>
</tr>
<tr>
<td>Live Litters</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total No.</td>
<td>21</td>
<td>23</td>
<td>24</td>
<td>23</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Implant sites</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total No.</td>
<td>232</td>
<td>265</td>
<td>266</td>
<td>265</td>
<td>274</td>
<td>266</td>
</tr>
<tr>
<td>Average/dam</td>
<td>11.0</td>
<td>11.5</td>
<td>11.4</td>
<td>11.5</td>
<td>11.4</td>
<td>11.1</td>
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<tr>
<td>Resorptions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total No.</td>
<td>4</td>
<td>9</td>
<td>4</td>
<td>8</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Dams with 1 or more sites resorbed</td>
<td>3</td>
<td>7</td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Dams with all sites resorptions</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>% partial resorptions</td>
<td>14.3</td>
<td>30.4</td>
<td>16.7</td>
<td>26.1</td>
<td>25.0</td>
<td>25.0</td>
</tr>
<tr>
<td>% complete resorptions</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Live Fetuses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total No.</td>
<td>227</td>
<td>256</td>
<td>261</td>
<td>257</td>
<td>264</td>
<td>258</td>
</tr>
<tr>
<td>Average/dam</td>
<td>10.8</td>
<td>11.1</td>
<td>10.9</td>
<td>11.2</td>
<td>11.0</td>
<td>10.8</td>
</tr>
<tr>
<td>Sex ratio(M/F)</td>
<td>0.86</td>
<td>0.91</td>
<td>0.63</td>
<td>0.67</td>
<td>0.87</td>
<td>0.73</td>
</tr>
<tr>
<td>Dead Fetuses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total No.</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dams with 1 or more dead</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dams with all dead</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% partial dead</td>
<td>4.76</td>
<td>-</td>
<td>4.17</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>% all dead</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Average Fetuses Weight g</td>
<td>3.67</td>
<td>2.53</td>
<td>3.80</td>
<td>3.81</td>
<td>3.87</td>
<td>3.86</td>
</tr>
</tbody>
</table>

- **Food/water consumption**
  No significant difference is found in comparison with to control.

- **Description, severity, time of onset and duration of clinical signs** : Not described

- **Gross pathology incidence and severity** :
  No clear effect on nidation, or on maternal or fetal survival

- **Fetal data**
  - **Grossly visible abnormalities**
    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.
Summary of skeletal findings

<table>
<thead>
<tr>
<th>Findings</th>
<th>Dose (mg/kg)</th>
<th>0</th>
<th>1.0</th>
<th>5.0</th>
<th>24.0</th>
<th>110.0</th>
<th>Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternebrae</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incompletd oss.</td>
<td>31/14</td>
<td>12/7</td>
<td>14/11</td>
<td>13/10</td>
<td>16/12</td>
<td>163/23</td>
<td></td>
</tr>
<tr>
<td>Bipartite</td>
<td>1/1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>3/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>105/22</td>
<td></td>
</tr>
<tr>
<td>Ribs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wavy</td>
<td>6/5</td>
<td>8/7</td>
<td>4/4</td>
<td>9/7</td>
<td>3/3</td>
<td>84/21</td>
<td></td>
</tr>
<tr>
<td>Less than 12</td>
<td>1/1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3/3</td>
<td></td>
</tr>
<tr>
<td>Vertebræ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incompletd oss.</td>
<td>2/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>127/23</td>
<td></td>
</tr>
<tr>
<td>Skull</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incompletd oss.</td>
<td>16/10</td>
<td>11/8</td>
<td>16/11</td>
<td>35/13</td>
<td>23/9</td>
<td>149/23</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyoid;missing</td>
<td>19/11</td>
<td>8/6</td>
<td>6/5</td>
<td>18/8</td>
<td>17/7</td>
<td>120/23</td>
<td></td>
</tr>
<tr>
<td>Hyoid;reduced</td>
<td>2/2</td>
<td></td>
<td>1/1</td>
<td></td>
<td>4/3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Numerator=Number of fetuses affected; Denominator= Number of litters affected

CONCLUSIONS

No teratological or other developmental effects were indicated in fetuses at any dose level.

DATA QUALITY

- Reliabilities: Reliable with restriction

REFERENCES (Free Text)


OTHER

- Last changed: September 2001
- Order number for sorting (administrative field)
TEST SUBSTANCE

- Identity: Disodium disulphite
  ⇒ Remarks: White crystalline material (FDA 71-22)

METHOD

- Method/guideline followed: Other
- GLP: No details
- Year: 1972
- Species: Rabbit
- Strain: Dutch
- Route of administration: oral (gavage)
- Doses/concentration levels: 1.23, 5.71, 26.5, 123 mg/kg bw
- Sex: Female
- Exposure period: day 6 - 18 of gestation
- Frequency of treatment: daily
- Control group and treatment: Negative control: sham treated controls
  Positive control: 2.5 mg/kg of 6-aminonicotinamide dosed on day 9
- Duration of test: 29 days of gestation
- Statistical methods: Not described

RESULTS

- NOAEL maternal toxicity: 123 mg/kg bw/day
- NOAEL teratogenicity: 123 mg/kg bw/day
- Maternal data with dose level: No clear effect on maternal toxicity
- Fetal data with dose level: No clear effect on fetal survival

REMARKS FIELD FOR RESULTS

- Reproduction data
  The administration of the disodium disulphite to pregnant rats had no clearly discernible effect on nidation, or on maternal or fetal survival.
- Body weight
No significant differences were found between treatment and negative control group.

- **Food/water consumption**
  No significant difference is found in comparison with control.

- **Description, severity, time of onset and duration of clinical signs**: Not described

- **Fetal data**
  - **Grossly visible abnormalities**
    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.

**CONCLUSIONS**

No teratological or other developmental effects were indicated in fetuses at any dose level.

**DATA QUALITY**

- Reliabilities: Valid with restriction

**REFERENCES (Free Text)**


**OTHER**

- Last changed: September 2001
- Order number for sorting (administrative field)
1) CHRONIC TOXICITY TO AQUATIC INVERTEBRATES (DAPHNIA)

TEST SUBSTANCE
- Identity: Disodium disulphite (CAS NO. 7681-57-4)
  ⇒ Remarks: Source: disodium disulphite, > 98 % (w/w), (BASF sulfite - factory RCA B 306)

METHOD
- Method: OECD TG202
- Test type: 21 days reproduction test
- GLP: YES
- Year: 1993
- Analytical monitoring: not stated
- Species/Strain/Supplier: Daphnia magna
- Test details: semi-static
- Statistical methods: Duncan’s multiple range test
  ⇒ Remarks:
  - Test organism:
    - Source, Supplier, any pretreatment, breeding method: The clone of Daphnia straus used was supplied by Institut National de Recherche Climique Appliquee, France, in 1978. The Daphnids are cultured under standard conditions in the laboratory
    - Age at study initiation: 2 - 24 hrs
  - Test condition:
    - Stock solution preparation: a defined amount of the test substance was weighed out and suspended directly in the test medium by stirring. The nominal concentration of the stock solutions were 100 mg/L
    - Test temperature range: 20 ±2°C
    - Exposure vessel type: numbered glass beakers nominal volume 100 mL, covered with numbered caps
    - Dilution water source: the synthetic medium M4
    - Dilution water chemistry: hardness = 2.20-3.20 [m mol/L ]; Ca: Mg = approx. 4:1; alkalinity up to pH 4.3 = 0.80-1.00 [m mol/L ]
    - Lighting- Day: Night rhythm 16:8 hours
    - Density of light: 5.6 μE/(m*m*s) in the range of 400-700 nm
    - Water chemistry in test: Oxygen content: 8.0 - 15.5 mg/L; pH=7.5 - 8.0
    - Feeding: Green algae (Scenedesmus subspicatus)
  - Element (unit) basis: reproduction
  - Test design: number of animals/vessel: 1, total number of animals/concentration: 10
  - Method of calculating mean measured concentrations: Not stated
  - Exposure period: 21 days
  - Analytical monitoring: Not stated

RESULTS
- Nominal concentration (as mg/L): 1.0, 5.0, 10.0
- Measured concentration (as mg/L): not determined
- Units (results expressed in what unit): mg/L
- Reproduction LC0 (21days) > 10.0 mg/L, NOEC (21days) > 10.0 mg/L
- Statistical results, as appropriate: by Duncan’s multiple range test, NOEC is >10.0 mg/L
  ⇒ Remarks:
● Biological observations
   - summary of the effect of the test substance on the reproduction of *Daphnia magna*. The values given are the mean, cumulative values for parent animals which survived the exposure for 21 days

<table>
<thead>
<tr>
<th>Conc. (mg/L)</th>
<th>Survival of parent animals</th>
<th>Live young per live parental animal</th>
<th>Dead young per live parental animal</th>
<th>Aborted eggs per live parental animal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>n ±1 SD</td>
<td>n ±1 SD</td>
<td>n ±1 SD</td>
</tr>
<tr>
<td>0.0</td>
<td>100</td>
<td>108.3 21.2</td>
<td>0.0 0.0</td>
<td>0.0 0.0</td>
</tr>
<tr>
<td>1.0</td>
<td>100</td>
<td>105.0 17.9</td>
<td>0.0 0.0</td>
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<tr>
<td>5.0</td>
<td>100</td>
<td>119.2 19.1</td>
<td>0.0 0.0</td>
<td>0.0 0.0</td>
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<tr>
<td>10.0</td>
<td>90</td>
<td>107.7 9.1</td>
<td>0.0 0.0</td>
<td>0.0 0.0</td>
</tr>
</tbody>
</table>

1SD*: 1 standard deviation

- Was control response satisfactory? : Yes

CONCLUSIONS

For Disodium disulphite, LC0 is 10.0 mg/L and NOEC is >10.0 mg/L. Experimental designs and results were well documented and prescribed conditions in the guideline were well satisfied.
 ⇒ Remarks :

DATA QUALITY

- Reliabilities : Reliable without restrictions.
 ⇒ Remarks :

REFERENCES (Free Text)


OTHER

- Last changed : September 2001
- Order number for sorting
 ⇒ Remarks :
2) SKIN IRRITATION

TEST SUBSTANCE

- **Identity**: Disodium disulphite – powder (CAS No. 7681-57-4)
- **pH**: 4.4 – 4.9 in a 20% solution of water
  - **Remarks**: Source: Hoechst AG purity: > 96%

METHOD

- **Method/guideline followed**: OECD TG 404
- **Type**: in vivo semiocclusivestudy
- **GLP**: yes
- **Year (study performed)**: 1981
- **Species/Strain**: Rabbit / Albino New zealand
- **Sex**: not specified
- **No. of animals**: 3
- **Total dose**: 500 mg of disodium disulphite
- **Vehicle**: 0.1 mL saline solution (NaCl 0.9 %)
- **Exposure time**: 4 hours
- **Grading scale**: Draize

REMARKS FIELD FOR TEST CONDITIONS

- **Controls**: none
- **Area of exposure**: about 24 h before treatment the dorsal surface (ca. 25 cm²) was shaved with electronic clippers. Only animals with intact skin were used.

RESULTS

Not irritating

- **Cumulative total and percent responders**: all 3 animals responded with slight erythema with an average score of 0.4. No edema was observed.

REMARKS FIELD FOR RESULTS

- **Numerical skin grades at 1, 24, 48 and 72 hours**:
  
  Individual Animal Grades for erythema and eschar
  1 h after patch removal (animal No. 1,2,3)
  0, 0, 0
  24 h after patch removal (animal No. 1,2,3)
  1, 1, 1
  48 h after patch removal (animal No. 1,2,3)
  0, 0, 1
  72 h after patch removal (animal No. 1,2,3)
  0, 0, 0

  No edema was observed.

- **Delayed grading scores at 7 to 14 days**: not necessary to perform
  - **Reversible effects**: all effects were reversible by 72 hours.
  - **Erythema/edema findings**: only erythema was observed.
- Other dermal lesion including systemic effects: none

CONCLUSIONS

The disodium disulphite was not irritating to the skin of the rabbit.

DATA QUALITY

- Reliabilities: Reliable without restriction

REFERENCES (Free Text)

Hoechst AG, Unpublished studies (87.1241), 11 Aug. 1987

OTHER

- Last changed (administrative field for updating): September 2001
- Order number for sorting (administrative field)
3) EYE IRRITATION

TEST SUBSTANCE

- **Identity**: Disodium disulphite – fine crystal powder (CAS No. 7681-57-4)
- **pH**: 4.4 – 4.9 in a 20% solution of water
  ⇒ Remarks: Source: Hoechst AG, Purity: > 96%, impurities: Na₂SO₃ (2%), Na₂SO₄ (2%)

METHOD

- **Method/guideline followed**: OECD TG 405
- **Type**: in vivo study
- **GLP**: yes
- **Year (study performed)**: 1987
- **Species/strain**: Rabbit / Albino New Zealand
- **Sex**: not specified
- **No. of animals per dose**: 3
- **Dose**: 100 mg/eye
- **Observation period**: 1, 24, 48, and 72 hours after application of the test substance, as well as 7 days after application.
- **Exposure time**: 24 hours
- **Scoring method used**: Draize

REMARKS FIELD FOR TEST CONDITIONS

- **Anesthetics**:
- **Vehicles**:
- **Eye washed**: rinsed after 24 hr exposure

RESULTS

- **Corrosive** (yes or no): no
- **Individual scores**: 1 h, 24 h, 48 h, 72 h, and 7 d for animals 1, 2, 3
  - **Conjunctiva chemosis**: 1 h: 3, 3, 3; 24 h: 2, 2, 3; 48 h: 1, 1, 2; 72 h: 1, 2, 2; 7 d: 1, 1, 3
  - **Conjunctiva redness**: 1 h: 2, 3, 3; 24 h: 3, 3, 3; 48 h: 3, 2, 3; 72 h: 3, 3, 3; 7 d: 2, 2, 3
  - **Iris**: 1 h: 1, 0, 1; 24 h: 1, 1, 1; 48 h: 1, 1, 1; 72 h: 1, 1, 1; 7 d: 1, 1, 1
  - **Corneal opacity**: 1 h: 1, 1, 1; 24 h: 2, 2, 2; 48 h: 2, 2, 2; 72 h: 1, 2, 2; 7 d: 2, 2, 3
  - **Corneal opacity fluor**: 24 h: 3, 1, 2; 72 h: 2, 4, 4; 7 d: 2, 3, 2

In addition, on day 7 corneal vascularization was slightly noticeable in two animals and clearly noticeable in one animal.

- **Overall irritation score**: not specified
- **Tool used to assess score**: additional evaluation of corneal opacity under UV light after fluorescein installation at the 24 and 72 hour time points, as well as after 7 days.
- **Description of lesions**: corneal opacity and vascularization of the cornea

REMARKS FIELD FOR RESULTS

- **Number of affected**: all animals
- **Score reduced time** (up to 21 days):
- **Reversible effect**: based on the effects seen after 7 days (corneal opacity and vascularization of the
CONCLUSIONS

The disodium disulphite was irritating to the eye in rabbit.

DATA QUALITY

- Reliabilities: Reliable without restriction

REFERENCES (Free Text)

Hoechst AG, Unpublished studies (87.1293), 21 Aug. 1987

OTHER

- Last changed (administrative field for updating): September 2001
- Order number for sorting (administrative field)
### 4) CARCINOGENICITY

**TEST SUBSTANCE**
- **Identity**: Disodium disulphite (CAS No 7681-57-4)
- **Remarks**: Source: Amsterdamsche Chinine Fabriek (ACF) - purity 95 ~ 99 % (as calculated from SO₂ determinations)

**METHOD**
- **Method/guideline followed**: Other
- **Test type**: Long-term feeding study
- **GLP**: No
- **Year**: 1971
- **Species**: Rat
- **Strain**: Wistar
- **Route of administration**: oral (feed)
- **Duration of test**: about 2 year
- **Doses/concentration levels**: 0, 0.125, 0.25, 0.5, 1.0, 2.0 %
- **Sex**: male & female
- **Exposure period**: 104 weeks (F0 and F1 generations), 30 weeks (F2 generations)
- **Frequency of treatment**: 7 days/week
- **Control group and treatment**: basal diet containing 0 % Na₂S₂O₅
- **Post exposure observation period**: None
- **Statistical methods**: Student’s t test and chi-square test

**REMARKS FIELD FOR TEST CONDITIONS**

- **Test Subjects**
  - **Age at study initiation**: Newly weaned rats
  - **No. of animals per sex per dose**: 20 animals/dose/sex
- **Study Design**
  6 experimental groups were maintained on a diet containing 0, 0.125, 0.25, 0.5, 1.0 and 2.0 % of disodium disulfite. 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. 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-generation 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 an 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 45 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. For more details of the method used see section 16.
  - **Vehicle**: none (stock diet containing the test substance)
  - **Satellite groups and reasons they were added**: none
  - **Organs examined at necropsy (macroscopic and microscopic)**
    Intermediate observation on organ weight and pathological changes.
    Mircoscopic: 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 lacrimal gland, aorta, mammary glands, uterus, prostate, seminal vesicle and
RESULTS

- **NOAEL (NOEL)**
  1.91 % as actual dose (942 Na$_2$S$_2$O$_5$ mg /kg bw/day)

- **Actual dose received by dose level**: The SO$_2$ determinations on the diets showed considerable losses of sulphite. Proportionally the losses of sulphite decreased with increasing dietary levels of sulphite as shown below table.

<table>
<thead>
<tr>
<th>Level of Na$_2$S$_2$O$_5$ added to diet(%)</th>
<th>Loss of Na$_2$S$_2$O$_5$ after storage for 1 week at –18 °C (%)</th>
<th>Actual dose level of Na$_2$S$_2$O$_5$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.125</td>
<td>22</td>
<td>0.098</td>
</tr>
<tr>
<td>0.25</td>
<td>14</td>
<td>0.215</td>
</tr>
<tr>
<td>0.5</td>
<td>12</td>
<td>0.44</td>
</tr>
<tr>
<td>1.0</td>
<td>8</td>
<td>0.92</td>
</tr>
<tr>
<td>2.0</td>
<td>5</td>
<td>1.91</td>
</tr>
</tbody>
</table>

REMARKS FIELD FOR RESULTS

- **General condition, mortality and growth**: The general condition of the rats remained good during the first 72 week in the F0-generation as well as in the two descendant generations. After this, aging symptoms developed in many rats and mortality increased rapidly in nearly all group. The survival in the sulphite groups was generally higher than in the controls, except in the case of males of the F1-generation given 2 % sulphite. No deaths occurred in the females of the same group.

- **Type and incidence of tumours**
  The number of lymphoreticular pulmonary tumours in males decreased with increasing levels of sulphite in the diet. The incidence of thyroid and pituitary tumours in the control group of the male rats 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 with no apparent relationship between number, location or type of tumours and the treatment.

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary level (%)</td>
<td>0 0.125 0.25 0.5 1 2</td>
<td>0 0.125 0.25 0.5 1 2</td>
</tr>
<tr>
<td>Total no. of rats with tumors</td>
<td>17 22 21 18 17 18</td>
<td>20 12 16 15 17 14</td>
</tr>
<tr>
<td>Lung: Malignant lymphoreticular tumor</td>
<td>10 10 8 6 6 3</td>
<td>2 5 4 5 2 4</td>
</tr>
<tr>
<td>Thyroid: Light-cell tumor: adenoma</td>
<td>1 8 6 4 8 5</td>
<td>4 5 5 4 3 7</td>
</tr>
<tr>
<td>Pituitary: Adenoma</td>
<td>0 5 5 1 4 4</td>
<td>8 2 4 3 4 0</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>0 2 1 2 2 2</td>
<td>0 1 1 1 0 0</td>
</tr>
<tr>
<td>Adrenal: Phaeochromocytoma Benign</td>
<td>6 4 8 5 1 7</td>
<td>1 0 4 1 2 2</td>
</tr>
<tr>
<td>Malignant</td>
<td>1 2 1 4 1 0</td>
<td>0 0 0 0 0 0</td>
</tr>
<tr>
<td>Cortical adenoma</td>
<td>0 0 0 1 0 0</td>
<td>0 0 0 0 0 0</td>
</tr>
<tr>
<td>Cortical carcinoma</td>
<td>0 1 0 0 0 0</td>
<td>0 0 0 0 0 0</td>
</tr>
<tr>
<td>Ovary granulose cell tumor</td>
<td>1 0 0 0 0 0</td>
<td>1 0 0 0 0 0</td>
</tr>
<tr>
<td>Uterus Polyp</td>
<td>3 3 4 3 3 3</td>
<td>3 3 4 3 3 3</td>
</tr>
<tr>
<td>Leukemia</td>
<td>3 1 2 0 0 0</td>
<td>2 0 1 0 2 0</td>
</tr>
</tbody>
</table>

CONCLUSIONS

Non-neoplastic observations were found in this study.

DATA QUALITY

- Reliabilities : Reliable with restrictions

REFERENCES (Free Text)