FOREWORD INTRODUCTION

# *METHANESULFINIC ACID, AMINOIMINO*

## *CAS N°: 1758-73-2*

# SIDS INITIAL ASSESSMENT PROFILE

| | |
|---|---|
| CAS NO | 1758-73-2 |
| CHEMICAL NAME | Methanesulfinic acid, aminoimino |
| STRUCTURAL FORMULA | NH<br>"<br>$HO_2S$-C-$NH_2$ |

RECOMMENDATION OF THE SPONSOR COUNTRY

[X] presently of low concern

[ ] needs further work

[ ] candidate for in-depth review a view to possible risk reduction activities

SHORT SUMMARY OF THE REASONS WHICH SUPPORT THE RECOMMENDATION

Environment:

Methanesulfinic acid, aminoimino (Formamidine sulfinic acid, FAS) is produced in a closed system, any dust or water releases are filtered off or decomposed during waste water treatment. Due to its limited stability and a calculated PEC/NEC ratio>1 FAS does not appear to be of significant environmental concern.

Human Health:

When the product is used as decolorization agent it decomposes to sulphate and urea. The amount of dust emitted is small, because the product for the customer is coarse grained. Aqueous aerosols of FAS are very toxic upon acute inhalation, acute oral toxicity is low, no organ-specific histopathological effects were noted. It is moderately irritating to the intact skin but there is no evidence of skin sensitization.

In conclusion FAS appears of little concern to human health provided that workers are appropriately protected from inhalation of FAS dust and from $SO_2$ forming during thermal decomposition.

# FULL SIDS SUMMARY

| CAS NO: 1758-73-2 | | SPECIES | PROTOCOL | RESULTS |
|---|---|---|---|---|
| **PHYSICAL-CHEMICAL DATA** | | | | |
| 2.1 | Melting Point | | | decomposition at 123°C |
| 2.2 | Boiling Point | | | |
| 2.3 | Density | | | 1680 kg/m³ |
| 2.4 | Vapour Pressure | | | < 0,36 Pa (at 30°C) |
| 2.5 | Partition Coefficient (log Pow) | | OECD TG104<br>ASTM D4629-86 | - 3,23 at 20°C |
| 2.6 A. | Water Solubility | | | 27 g/l at 20°C |
| B. | pH-Value | | | 4,0 at 10 g/l (at 20°C) |
| | pKa-Value | | | |
| 2.12 | Oxidation: Reduction Potential | | | |
| **ENVIRONMENTAL FATE AND PATHWAYS** | | | | |
| 3.1.1 | Photodegradation | | | |
| 3.1.2 | Stability in Water | | | degradation in contact with air >30% (22 hr) |
| 3.2 | Monitoring Data | | | in air = < 0,5 mg/m³<br>in waste water = < 10 mg/l |
| 3.3 | Transport and Distribution | | Calculated (Fugacity Level 1 type) | |
| 3.5 | Biodegradation | | (local exposure)<br>NEN 3235/5.4 | 71 %, BOD 0,42 mg $O_2$/l |
| **ECOTOXICOLOGICAL DATA** | | | | |
| 4.1 | Acute/Prolonged Toxicity to Fish | Poecilia reticulata | OECD TG203 | $LC_{50}$ (96 hr) = 416 mg/l<br>NOEC=180 mg/l |
| 4.2 | Acute Toxicity to Aquatic Invertebrates *Daphnia* | Daphnia magna | OECD TG202 | $EC_{50}$ (24 hr) = 390 mg/l<br>NOEC=180 mg/l |
| 4.3 | Toxicity to Aquatic Plants e.g. Algae | Scenedesmus subspicatus | OECD TG201 | $EC_{50}$ (72 hr) = 32 mg/l<br>NOEC=27 mg/l |
| 4.5.2 | Chronic Toxicity to Aquatic Invertebrates (Daphnia) | | | |
| 4.6.1 | Toxicity to Soil Dwelling Organisms | | | |
| 4.6.2 | Toxicity to Terrestrial Plants | | | |
| (4.6.3) | Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds) | | | |

# FULL SIDS SUMMARY
## PART 2

| CAS NO: 1758-73-2 | | SPECIES | PROTOCOL | RESULTS |
|---|---|---|---|---|
| **TOXICITY** | | | | |
| 5.1.1 | Acute Oral Toxicity | rat, Spra.Daw. | Litchfield -Wilcoxon | $LD_{50}$ = 1120 mg/kg |
| 5.1.2 | Acute Inhalation Toxicity | rat, S.D. | OECD TG403 | $LC_{50}$ = 0,164 mg/l/4 hr |
| 5.1.3 | Acute Dermal Toxicity | rat, S.D. | OECD TG402 | $LD_{50}$ > 2000 mg/kg |
| 5.4 | Repeated Dose Toxicity | rat, Wistar | OECD TG407 | NOEL=47 mg/kg |
| 5.5 | Genetic Toxicity In Vitro | | | |
| A. | Bacterial Test (Gene mutation) | S.typhi. | OECD TG471 (Ames-Test) | with met. act.= + without met. act.= + |
| B. | Non-Bacterial In Vitro Test (Chromosomal aberrations) | | | |
| 5.6 | Genetic Toxicity In Vivo | mouse | OECD TG474 | genotoxic effects= – |
| 5.8 | Toxicity to Reproduction | rat, Wistar | OECD TG421 | NOEL=47 mg/kg (R.T.P) NOEL=15 mg/kg (R.T.F1) |
| 5.9 | Developmental Toxicity/ Teratogenicity | | | |
| 5.11 | Experience with Human Exposure | | | |

[Note] Data beyond SIDS requirements can be added if the items are relevant to the assessment of the chemical, e.g. corrosiveness/irritation, carcinogenicity.

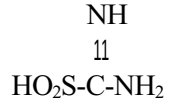
| | | |
|---|---|---|
| Toxicity to bacteria | Pseudomonas putida<br>toxicity threshold value: 538 mg/l | NEN 6509 |
| Skin irritation | Albino rabbit (New Zealand white) patch-test<br>average scores after 72 hours: intact skin 3.3<br>abraded skin 5.3 | |
| Eye irritation | Albino rabbit (New Zealand white)<br>maximum scores after 7 days: cornea 2-3, iris 1<br>conjunctivae redness 1<br>conjunctivae chemosis 2 | FDA |
| Mammalian cell gene mutation test | chinese hamster ovary cells<br>with metabolic activation = –<br>without metabolic activation = – | OECD 476 |

# SIDS INITIAL ASSESSMENT REPORT

**CAS No.** 1758-73-2

**CHEMICAL NAME** **Methanesulfinic acid, aminoimino**

**STRUCTURAL FORMULA**



## General Information

Formamidine sulfinic acid (FAS) is a white powder which is soluble in water (max. 27 g/l) [1]. It decomposes upon heating > 50℃ [2] and spontaneously beyond 100℃ (exotherm) with formation of $SO_2$. The partition coefficient octanol/water is low: log $P_{OW}$ -3,23 [3]. Also the vapour pressure is low: < 0,36 Pa at 30℃ [4].

FAS is manufactured at a single plant in Austria [5]. Production levels reported are 1000-5000 t/year. Production of FAS in other countries is not known. FAS is manufactured mainly for use in industrial purposes. It is a strong reductant and is used to discolour dyes in paper recycling, textile printing and similar processes. During use, the product decomposes to sul-fate and urea.

## Environment

Exposure: Release to waste water treatment plant at the production site is between 160 and 645 kg FAS/day [6]; measured data on release at customer plants into waste water are not available. When the product is used, it degrades to sulfate and urea. FAS decomposes in wa-ter (> 30% in 22 h) [7] and is biodegradable [8]. It is not toxic to bacteria. Because of its low par-tition coefficient octanol/water no potential for bioaccumulation is expected.

Discharge into air at the production site is < 1 mg FAS/$m^3$ and < 0,5 kg/day [9]. Discharge of FAS dust from plants where FAS is used is expected to be small, because the product is coarse grained.

Environmental distribution and exposure have been modelled using the USES V 1.0 NL program. Daily local emissions from Sewage treatment plant into air were calculated to be 0,18, to water 9,2; to suspended matter 3,4 x $10^{-8}$ and to sludge 8 x $10^{-6}$, all in kg.

Effects: FAS is of low aquatic- toxicity. With fish (Poecilia reticulata) an $LC_{50}$/96 h value of 416 mg/l was found in a semistatic procedure, at 48 h toxicity was lower ($LC_{50}$ approx 700 mg/l) [10]. Immobilization of Daphnia magna occured with an $EC_{50}$ of 390 mg/l [11]. Growth inhibition of the alga Scenedesmus subspicatus was obtained with an $EC_{50}$ (72 h) of 32 mg/l. Below 27 mg/l a stimulation of growth was seen, and a NOEC of 7,5 mg/l (inclu-ding the stimulatory effect) was calculated [12]. Inhibition of multiplication of bacterium Pseu-domonas putida was found beyond a "toxicity threshold" value of 538 mg/l [13].

In conclusion, because of low bioaccumulation potential, limited stability in water, low levels of exposure and a low toxicity to aquatic organisms this chemical shows low environ-mental concern. The probability for PEC/NEC > 1 is 0,2858 (calculated with USES v. 1.0).

Biodegradability

The procedure was carried out in conformity with NEN 3235 section 5.4 (Nether-lands Normalisatie Institute NNI, Rijswijk, 1972). The study was not performed under GLP regulations. Formamidine sulfinic acid was tested for bacterial degradability at concentra-tions of 2,0 and 10,0 mg/l; as microbiotic source an inoculum was obtained from a local municipal sewage treatment plant. After incubation for 5 days in a closed bottle the oxygen consumption was determined (biochemical oxygen demand - BOD). With 2 mg sodium acetate which served as positive control a BOD of 58% of the theoretical oxygen demand was found. With formamidine sulfinic acid the BOD was 71% and 57% for the low and high concentration, respectively. It was concluded that formamidine sulfinic acid appeared not be toxic to the microorganisms in the inoculum. Furthermore the study shows that the test compound is degradable under the conditions of the test.

Chemical Oxygen demand

102,5mg Formamidine sulfinic acid (FAS) was dissolved in 100ml Milli-Ro water. 10ml of this stock solution and 10ml Milli-Ro water were brought into a 250ml round bottom flask. After the addition of anti bumping stones, 2ml sulphuric acid (18 M), 10ml potassium dichromate (0,04 M) and 30ml sulphuric acid, containing silver sulphate, the solution was boiled under reflux for two hours. The remaining potassium dichromate was thereafter titrated, using a freshly normalised ferrous(2)ammonium sulphate (0,104 M) solution and ferroin solution as an indicator. A blank, containing 10ml Milli-Ro water instead of 10ml test substance stock solution, was run simultaneously. The test was performed in triplicate (0,410 g COD/g FAS, 0,415 g COD/g FAS, 0,420 g COD/g FAS)

Stability in air and in water

An aqueous solution of 1 g formamidine sulfinic acid/l water was contacted with air (380 ml/min) at 20℃. The pH-value of this solution decreased from a pH of 6,9 to 5,4 after 22 hours. The reference sample shows, that the pH of drinking water (8E dH) increased under the test conditions from 7,1 to 8,5. This is caused by removal of $CO_2$. Therefore the building rate of acid in the formamidine sulfinic acid solution is higher than indicated by the decrease of the pH-value.

Toxicity to fish

Formamidine sulfinic acid was tested in conformity with OECD guideline 203, April 4, 1984. Young guppies of 1-3 cm length were exposed to various concentrations of the test compound for 96 hours. They were not fed for 24 hours prior to test and throughout the test period. Test media were renewed at each 24 hour interval (semistatic procedure). The con-centrations tested were 0; 100; 180; 320; 560 and 1000 mg/l; they had been selected on the basis of a preliminary test in which groups of 5

fish were exposed to a range between 0,1 and 1000 mg/l. In the main study after 48 hours 100% mortality was observed at 1000 mg/l; 10% mortality at 560 mg/l and no mortality at lower concentrations. After 96 hours 80% mortality was seen at 560 mg/l and 20% mortality at 320 mg/l. In addition increased pigmentation and decreased swimming ability were recorded at 320 mg/l and higher. The 96-hour-$LC_{50}$ was 416 mg/l, the NOEC was 180 mg/l.

Toxicity to daphnids

Formamidine sulfinic acid was tested in conformity with OECD guideline 202 of April 4, 1984. Less than 24 hours old Daphnia magna animals were exposed to various concentrations of the test compound for 24 hours. Concentrations tested were selected on the basis of preliminary tests and were between 100 to 1000 mg/l. At least 10 animals were exposed to each concentration. Potassium dichromate was used as a positive control, with which an $EC_{50}$ value between 1,0 and 1,8 mg/l was found. This was in the expected range and confirmed the validity of the test system. Furthermore in the control vessels immobi-lization did not exceed 10%. It was found that 100% immobilization by formamidine sulfinic acid occurred at 1000 mg/l, the No-Observed-Effect-Concentration (NOEC) was 180 mg/l and the $EC_{50}$ was 390 mg/l.

Toxicity to algae

The effect of formamidine sulfinic acid on growth of the fresh water green algae Scenedesmus subspicatus was studied according to OECD guideline 201, June 7, 1984. The test was performed on exponentially growing cultures of the algae; cell numbers were counted at the beginning of incubation and then after 24, 48 and 72 hours. Potassium di-chromate served as a positive control; it was inhibitory on algae growth rate with an $EC_{50}$ of approximately 0,5 mg/l demonstrating the validity of the test system. In a range finding test with formamidine sulfinic acid almost complete inhibition of the algae growth was found between 64,2 and 116,5 mg/l; the $EC_{50}$ was estimated graphically to occur in the range of 25,7 to 64,2 mg/l. Therefore in the main test concentrations in the range between 0 and 64 mg/l were used. HPLC analysis and UV photometry revealed that the compound decomposed over the testing period of 72 hours. Therefore $EC_{50}$ calculations were per-formed with the nominal test substance concentrations. The main test for effects of formamidine sulfinic acid an algae growth was performed in triplicate. Inhibition of greater 90% was found at 64 mg/l. The $EC_{50}$ was 32,0 mg/l. The No-Observed-Effect concen-tration for growth inhibition was 27 mg/l. At lower concentrations there appeared to be a stimulation of growth for which a No-Observed-Effect concentration of 7,5 mg/l was calculated.

Toxicity to bacteria

Formamidine sulfinic acid was evaluated for its ability to inhibit cell multiplication of the bacteria species pseudomonas putida. It was conducted in compliance with GLP regulations. Cultures of the bacteria were exposed to concentrations between 0,5 and 1000 mg test compound/l and were incubated for 18 +/- 2 hours at 25℃. Cell number was estimated by turbidity measurement at 436 nm. Methanol was used as a positive control, and a "toxicity threshold" of 17,7 mg/l was found; it was concluded that the test system was valid. With formamidine sulfinic acid a toxicity threshold value of 538 mg/l was found.

**Human Health**

Human exposure: Exposure may occur at the workplace, mainly by inhalation of FAS dust. At the Austrian production plant 6 workers can be exposed to 0,2-2,4 mg FAS dust/$m^3$ [14] (mean/shift). Exposure at work places of industrial users is expected to be low, because the product for customer use is coarse grained to reduce dust emissions. Due to the low vapour pressure no relevant exposure to FAS vapour is to be expected. There is no known direct exposure of the general consumer except in Switzerland, where FAS is on market in small quantities.

Potential indirect exposure was modelled by means of the USES V 1.0 NL program; a total human dose of 2,153 x $10^{-7}$ mg/kg daily was calculated.

Health effects: Aqueous aerosols of FAS were very toxic upon acute inhalation ($LC_{50}$ 0,164 mg/l/4 h in rats) [15]; at histopathological examination the lung, nasal cavity and trachea showed inflammation, haemorrhage, edema and fibrosis in all treated groups, including the low dose group (59 mg/$m^3$ air). No repeated dose inhalation study is available in the SIDS. Acute oral toxicity of FAS is low ($LD_{50}$ 1120 mg/kg in rats) [16]. Repeated oral application of FAS to rats for 4 weeks on 5 days/week revealed a NOEL of 47 mg/kg [17]. Higher doses produced various signs of intoxication, but no organ-specific histopathological effects were noted. There was no acute dermal toxicity ($LD_{50}$ > 2000 mg/kg in rats) [18]. FAS was mode-rately irritating to the intact skin and severely irritating to the abraded skin and to eyes in rabbits [19, 20]. There was no evidence of skin sensitization in guinea pigs [21].

Studies on genetic toxicity showed a weakly mutagenic effect in Salmonella strains TA 1535 and TA 100 with and without metabolic activation (the study was reported in 1981 and did not conform to OECD guidelines and GLP principles) [22]. No mutagenic activity of FAS was detected in a mammalian cell system (CHO cells with and without metabolic activation) which was performed according to current OECD guidelines with GLP [23]. Of 4 micronucleus tests performed with FAS in vivo in mouse bone marrow one single test was weakly positive but the validity of this study was in question [24]. It was concluded that the weight of evidence clearly supported non-mutagenicity of FAS in mouse bone marrow in vivo. Adverse effects on reproduction of rats were found after doses of 150 mg/kg changed to 47 mg/kg after 11 days of treatment, i.e. 3 days before mating because of maternal toxicity at 150 mg/kg. Ad-verse effects were lower mean number of corpora lutea/dam and lower mean total litter size/dam at birth. No maternal or reproductive toxicity was noted to 5 mg/kg on day 12. Al-though it could not be excluded that reproductive toxicity seen after 150/47 mg/kg was due to the initial high dose, the NOEL was considered to be 15 mg/kg [25].

No documented effects of FAS on human health are known to us.

In conclusion FAS appears of little concern to human health provided that workers are appropriately protected from inhalation of FAS dust and from $SO_2$ formed during thermal decomposition. In Switzerland any products available to the general consumer are labelled as "Giftklasse 2" corresponding to "toxic". The margins of safety for humans were calculated by modelling to be 9 x $10^3$ locally and 2 x $10^8$ regionally.

Acute oral toxicity

The test was performed before guidelines and GLP regulations were developed. Groups of 5 male and 5 female Sprague Dawley rats each received formamidine sulfinic acid at 5 different doses once orally by gavage. Doses used are not indicated. Signs of intoxication were sedation, ataxia, lying on belly or flank, hypoventilation and reduced reflexes beginning after 6 to 8 hours. Death occured within 18 to 72 hours. After necropsy there was possibly lung edema. The $LD_{50}$ was calculated according to Litchfield and Wilcoxon at 1120 mg/kg. "Toxicity threshold" is reported to be approximately at 900 mg/kg.

Acute inhalation toxicity

Formamidine sulfinic acid was tested according to OECD guideline 403 of May 12, 1981. Groups of 5 male and 5 female Sprague Dawley rats (Him:OFA) each were exposed for 4 hours to air containing 59, 117 and 229 mg formamidine sulfinic acid per $m^3$ air in a nose-only inhalation device. For this purpose a watery solution of the test compound was nebulized; the actual concentrations in the aerosol were determined 9 or 10 times during each inhalation period. In the high concentration group all animals died 1 or 2 days after treatment. In the mid concentration group there was temporary loss of body weights during the first week. Observations in life included ruffled fur, chromodacryorrhea and difficulties in breathing in all mid and high-dosed animals. In the low dose group difficulties in brea-thing were hardly detected. Anemia and cyanosis as well as low locomotion were found in some mid- and high-dosed animals. At terminal necropsy no lesions were found in 5/10 animals of low-dosed group: in all other animals, haemorrhages or white coverings were found in the lungs, the severity depending on the concentration. Histopathology revealed a corrosive action of test compound in the lung as indicated by multifocal fibrosis, inflam-mation, proliferation, edema, congestion, loss of cilia etc. Some of these changes were present in the low-dose group and increased with increasing doses. Trachea and nasal cavity were also affected. An $LC_{50}$ of 0,164 mg/l/4 hrs was calculated.

Acute dermal toxicity

Formamidine sulfinic acid was tested according to OECD guideline 402, February 24, 1987. 5 male and 5 female Sprague Dawley rats (Him:OFA) were hair-clipped and received 1 day later a dermal dose of 2000 mg formamidine sulfinic acid/kg body weight. Application was achieved by spreading the test substance over an area of approx. 5 x 6 cm and moistening with destilled water. The area was then covered by a cellulose patch for 24 hours. The only adverse in-life-observation was chromodacryorrhea which occurred maxi-mally 1 day after administration of the compound in all males and 4/5 females. This was attributed to reduced well-being caused by the dressing. At necropsy no changes were observed that could unequivocally be attributed to the test compound. It is concluded that the $LD_{50}$ (dermal) of formamidine sulfinic acid is beyond 2000 mg/kg b.w.

Skin Irritation

The test was performed in 1981. 12 New Zealand white rabbits were hair-clipped and in 6 of them the skin was abraded. 0,5 g of the test compound (a 40% mixture with water) was brought on the intact

or abraded skin under a surgical patch of 1 inch x 1 inch which was left in place for 24 hours. At this time and 48 hours later lesions were evaluated ac-cording to Draize or to an institute-own grading system. At both time points it was found that formamidine sulfinic acid was moderately irritating to the intact skin and severely irritating to the abraded skin.

Eye Irritation

Formamidine sulfinic acid was tested for eye irritation according to procedures pu-blished by the FDA (1963) and Draize and Kelley (1952). 6 New Zealand white rabbits received a treatment with 100 mg of the test compound on the everted lower lid of one eye. After 24 hours slight opacity of the cornea, slight iritis and moderate redness and slight to severe swelling of the conjunctivae were noted. In the course of the 7 day observation period some of these effects recovered partly or completely. However, at 7 days slight to severe cornea opacity and vascularization of the cornea were observed in 4 rabbits, ulcus cornea in 2 rabbits, slight iritis in 3 rabbits and slight lesions of the conjunctivae in all rabbits. It was concluded that according to the FDA standards formamidine sulfinic acid was a severe eye irritant.

Skin sensitisation

Formamidine sulfinic acid was injected daily for 10 days intracutaneously into the hair-clipped skin of guinea pigs. The strain of guinea pigs used had previously been shown to be responsive to sensitization by 2,4-dinitrochlorobenzene. The doses of the test com-pound injected were selected to produce no local reactions, and the place of injection was altered daily. After further 10 days without treatment the test compound was again injected intracutaneously on 2 subsequent days, and 24 and 48 hours later local reactions were re-gistered. There were no reactions observed exceeding those of physiological saline which served as negative control. It was concluded that formamidine sulfinic acid had no sensi-tizing effect under the conditions of the present study.

Repeated dose toxicity

Formamidine sulfinic acid was tested according to OECD guideline 407 of May 12,1981. Groups of 5 male and 5 female Wistar rats each received once per day on 5 days per week during 4 consecutive weeks an oral dose of the test compound per gavage. Doses were 0, 15, 47 and 150 mg/kg body weight per day. These doses were selected on the basis of a preliminary study in which 80, 240 or 720 mg test compound/kg b.w. had been admi-nistered to rats for 7 consecutive days. In this preliminary study the high dose caused death of 9/10 animals and 240 mg/kg caused significant loss of body weight, lower food consumption and thymus atrophy in all animals. In the main study no deaths occurred. Changes observed in the high dose group (150 mg/kg) included reduced body weight gain, reduced food consumption, raised fur, reduction of serum levels of cholesterol, glucose and alkaline phosphatase, elevation of serum levels of bilirubin and inorganic phosphate, re-duced weights of the thymus. In the mid dose group only a decrease of serum alkaline phosphatase was found. Histopathological analysis did not reveal unequivocally substance related effects. Since the decreased alkaline phosphatase at the mid dose level was an iso-lated effect it was concluded that the No-Adverse-Effect-Level was 47 mg formamidine sulfinic acid per kg body weight in both sexes of rats.

Bacterial test

Test performance was similar to OECD guideline 471. The specific tests performed were not subjected to inspection for quality assurance although the processes involved were inspected at predetermined intervals. The report was audited by IRI quality assurance per-sonal according to SOP. Formamidine sulfinic acid was tested for mutagenic activity in an Ames test using Salmonella typhimurium strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100 and Escherichia coli strain WP2 uvrA$^-$ (pKM101). All tests were performed with and without metabolic activation system (S 9 mix from arochlor-treated male Sprague Dawley rats). Adequate positive and negative controls were used in some but not all tests performed and where studied showed the validity of the test system. Formamidine sulfinic acid was tested in concentrations of 33,3; 100; 333,3; 1000; 3300 and 10000 g /plate. In a second series of experiments 0,75; 1; 2,5; 5; 7,5 and 10 mg/plate were used. At 1000 and more g/plate the test compound was not completely dissolved. 5 mg/plate and more pro-duced bacterial toxicity. It was found that formamidine sulfinic acid was weakly mutagenic to strain TA 1535 and TA 100 suggesting base-pair substitution mutations. Mutagenicity was detected in the presence and absence of S 9 mix and the lowest concentration causing a mutagenic effect was 0,75 mg/plate.

Mammalian cell gene mutation test

Formamidine sulfinic acid was tested according to OECD guideline 476 of April 4, 1984, Chinese hamster ovary (CHO) cells were treated with formamidine sulfinic acid in the absence and presence of an exogenous metabolizing system (S 9 mix from arochlor-treated rats). Formation of mutations in the HGPRT-locus were checked by the ability to form colonies in selection medium containing 6-thioguanine. The validity of the test sys-tem was confirmed by positive and negative controls. Concentrations of the test compound used were between 50 and 800 mg/l; two independent experiments were performed. At concentrations exceeding 400 mg/l cytotoxicity was observed in the absence of exogenous metabolizing system. At none of the concentrations tested a clear increase of mutant colo-nies was obtained. It was concluded that formamidine sulfinic acid was not mutagenic in the present test system.

Non-bacterial test in vivo

Formamidine sulfinic acid was assessed in the micronucleus assay for its possible potential to induce micronuclei in polychromatic erythrocytes (PCE) in the bone marrow of the mouse with a dose of 600 mg/kg b.w. (at 24 h, 48 h and 72 h preparation interval). 600 mg/kg b.w. formamidine sulfinic acid was estimated by pre-experiments to be the maxi-mum attainable dose. The animals expressed slight toxic reactions.

The mean number of normochromatic erythrocytes was not increased after treatment with formamidine sulfinic acid as compared to the mean values of NCEs of the negative control, indicating that formamidine sulfinic acid had no cytotoxic properties in the bone marrow.

There was no enhancement in the frequency of the detected micronuclei in compa-rison to the negative control at any preparation interval after administration of formamidine sulfinic acid.

30 mg/kg b.w. cyclophosphamide administered per os was used as positive control which showed a statistically significant increase of induced micronucleus frequency.

Subacute and reproductive toxicity

This study was performed as a screening test to evaluate adverse effects on reproduc-tive performance associated with repeated administration of formamidine sulfinic acid, according to OECD guideline 421 (final draft). Formamidine sulfinic acid was admini-stered orally by gavage to 3 groups (low dose, mid dose, high dose) of 12 male and 12 female Wistar rats each once a day. An equally sized negative control group was treated with the vehicle. The test substance was administered freshly dissolved in distilled water at a dose volume of 10 ml per kg body weight. Doses of 0 (control), 15 (low dose), 47 (mid dose) and 150 mg (high dose) test substance per kg body weight and day were used up to day 11 and were reduced to 5 (low dose), 15 (mid dose) and 47 (high dose) mg/kg there-after due to severe test substance effects. Mating was performed on an 1:1 base after 2 weeks of premating period. Couples were separated after successful mating resp. at the end of 10-days mating period. Dams were allowed to litter normally and were sacrificed to-gether with their offspring on day 4 of lactation. Dosing was started at beginning of pre-mating period and continued until termination of the study.

Investigations performed:

Parental animals: Observations in life; body weight; feed consumption; mating results; time of parturition; necropsy; organ weight analysis; histopathology of selected tissues. Offspring: Observation in life; litter weight; number; sex and viability; necropsy.

The test substance caused severe systemic toxic changes in the high dosed animals at a dose of 150 mg/kg body weight (lower mean body weight, body weight loss, reduced feed consumption, signs of reduced well-being like emaciation, yellow and reduced faeces). After reduction of all doses to a third of the initial doses from day 12 on the animals of the high dose group slowly recovered from most adverse effects, but not from all (e.g. signi-ficantly lower body weight). No toxic signs were observed in the low and mid dose group, neither before dose reduction nor thereafter. No treatment related histopathological changes or gross changes were found.

Concerning toxic effects of the test substance, the No-Observed-Adverse-Effect-level in this study for both sexes is therefore considered to be 47 mg formamidine sulfinic acid per kg body weight, when administered daily on seven days per week.

Parameters of fertility like time until conception, duration of pregnancy or fertility index were unaffected by treatment with the test substance. Significant effects of the test substance on reproduction were a lower mean number of corpora lutea per dam and a lower mean total litter size per dam at birth in the high dose group, compared to the negative con-trol group. These effects are probably caused by maternal toxicity at the initial high dose of 150 mg/kg. Nevertheless, adverse effects on reproduction cannot be excluded at the re-duced high dose of 47 mg/kg, Therefore the No-Observed-Adverse-Level for reproductive performance is considered to be 15 mg formamidine sulfinic acid per kg body weight under the conditions of this study.

**Conclusions and recommendations**

FAS is mainly used for industrial purposes and no direct exposure of the general con-sumer is expected in most countries. Inhaled aqueous aerosols of FAS were highly toxic to rats. Therefore, adequate protection of workers and customers from inhalation of FAS is required at the work place. Estimated exposures of workers at the Austrian production site are lower (at least 25 fold) than toxic doses in animals. Exposures are expected to be even lower at work places of industrial customers. No potential human health risks are envisaged provided that appropriate measures to protect from inhalation of dust are taken at the work place. In countries where general consumers have access to FAS, appropriate labelling of the pro-duct as "very toxic" by inhalation should be required. Due to its limited stability, extremely low $P_{OW}$, low toxicity to water organisms, low environmental exposure and a calculated probability of 0,2858 for PEC/NEC ratio > 1 FAS does not appear to be of significant environmental concern.

It is recommended that adequate protective measures are taken. No further testing of FAS is required as long as its use pattern and the exposure situation remain unchanged.

**References:**

1 OECW - Degussa Austria Ges.m.b.H., A-9721 Weißenstein, Health & Safety Data Sheet 11.12.1989
2 OECW - Degussa Austria Ges.m.b.H., A-9721 Weißenstein, IUCLIC Data Sheet 7.8.1995
3 ÖMV-AG, A-2320 Schwechat, report order no. AN9207
4 ÖMV-AG, A-2320 Schwechat, report order no. AN9207 (26.2.1992)
5 OECW - Degussa Austria Ges.m.b.H., A-9721 Weißenstein, IUCLID data sheet 7.8.1995, exposure assessment 2.9.1992, 9.8.1996,
6 OECW - Degussa Austria Ges.m.b.H., A-9721 Weißenstein, IUCLID data sheet 7.8.1995, exposure assessment 2.9.1992, 9.8.1996,
7 OECW - Degussa Austria Ges.m.b.H., A-9721 Weißenstein, Test report Jan. 26, 1994
8 Degussa AG, unpublished, report no.: US-IT-Nr. 89-0019-DKO (1989)
9 Dipl.Ing. Dr. D. Wewerka, A-8010 Graz, report No. 79/93-849 (1993), Österreichische Staub- (Silikose-) Bekämpfungsstelle, Leoben, Austria, report 20.12.1993
10 Degussa AG, unpublished, report no.: US-IT-Nr.: 88-0049-DGO (1988)
11 Degussa AG, unpublished, report no.: US-IT-Nr.: 88-0048-DGO (1988)
12 Agrolinz Ges.m.b.H. A-4060 Leonding, report no. 1136 (July 1992)
13 Degussa AG, unpublished, report no.: US-IT-Nr.: 88-0044-DGO (1988)
14 Dipl.Ing. Dr. D. Wewerka, A-8010 Graz, report No. 79/93-849 (1993), Österreichische Staub- (Silikose-) Bekämpfungsstelle, Leoben, Austria, report 20.12.1993
15 Österreichisches Forschungszentrum Seibersdorf, A-2444 Seibersdorf (September 1992)
16 Degussa AG, unpublished, report no.: US-IT-Nr.: 70-0004-DKT (1970)
17 Österreichisches Forschungszentrum Seibersdorf, A-2444 Seibersdorf (July 1992)
18 Österreichisches Forschungszentrum Seibersdorf, A-2444 Seibersdorf (March 1992)
19 TNO, NL-3700 AJ Zeist, project no. B81-0061-35
20 TNO, NL-3700 AJ Zeist, report no. V 81.353/210061
21 Degussa AG, unpublished, report no.: US-IT-Nr.: 70-0003-DKT (1970)
22 Inveresk Research International, EH21 7UB Musselburgh Scotland, IRI project no. 705022 (July 1981)
23 Österreichisches Forschungszentrum Seibersdorf, A-2444 Seibersdorf (December 1992)
24 Research & Consulting Company Ltd., CH-4452 Itingen, project no. 007244 (April 1982)
Microtest Research Limited, Y01 5 DU York, United Kingdom; Report Ref: 31MRESTO.005 (1989)
Österreichisches Forschungszentrum Seibersdorf, A-2444 Seibersdorf, (June 1994)
Degussa AG, unpublished, report no.: US-IT-Nr.: 95-0048-DGM (1995)
25 Österreichisches Forschungszentrum Seibersdorf, A-2444 Seibersdorf, (June 1993)

# Full SIDS Dossier

## 1. Chemical Identity

**CAS-number** 1758-73-2

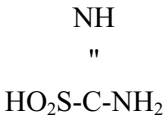
**Name** Methanesulfinic acid, aminoimino

**Common Synonyms**

Formamidine sulfinic acid
Formamidinsulfinsre
Aminoiminomethansulfinsre
Thiourea dioxide
Thioharnstoffdioxid

**Empirical formula** $CH_4N_2O_2S$

**Structural formula**



**Degree of purity (percentage by weight)** > 99 % w/w

**Identity of major impurities** Thiourea

## 2. Physical-Chemical Data

**Melting or Decomposition Point** spontaneous exothermic decomposition at 123℃

GLP: YES **[ ]**
NO **[X]**

Comments: Decomposition
on lengthy exposure of heating > 50°C

Reference: OECW - Degussa Austria Ges.m.b.H.,
A-9721 Weißenstein, IUCLID Data Sheet 7.8.1995

**Vapour pressure** < 0,36 Pa at 30°C

Method: OECD GUIDELINE NO.:104

GLP: YES **[ ]**
NO **[X]**

Comments: Formamidine sulfinic acid was determined via the $N_2$ assay. The limit of the analytical system according to ASTM D4629-86 and SOP-LM Nr. AN 0025 was the concentration of the control analysis. No increase could be found, therefore the vapor pressure was estimated < 0,36 Pa.

Reference: ÖMV-AG, A-2320 Schwechat, report order no. AN9207 (26.2.1992)

**Partition coefficient n-Octanol/water**

log Pow = -3,23 at 20°C

Method: calculated **[ ]**
measured **[X]**

GLP: YES **[ ]**
NO **[X]**

Analytical Method: ASTM (see Comments)

Comments: The OECD-Guideline 117 is only practicable for partition coefficients 0-6, the OECD-Guideline 107 is only practicable for partition coefficients 2-4, therefore for $N_2$ determination (for calculating formamidine sulfinic acid) the methods ASTM D4629-86 and SOP-LM Nr. AN 0025 were used.

Reference: ÖMV-AG, A-2320 Schwechat, report order no. AN9207

**Water solubility** 27 g/l at 20°C

GLP: YES **[ ]**
NO **[X]**

Reference: OECW - Degussa Austria Ges.m.b.H.,

A-9721 Weißenstein,
Health & Safety Data Sheet 11.12.1989

**pH in water** pH: 4 at 10 g/l (water)

Method (e.g., OECD, others):

GLP: YES **[ ]**
NO **[X]**

Reference: OECW - Degussa Austria Ges.m.b.H.,
A-9721 Weißenstein,
Health & Safety Data Sheet 11.12.1989

**Relative density (4/20)** 1,68 g/cm$^3$

Reference: OECW - Degussa Austria Ges.m.b.H.,
A-9721 Weißenstein,
Health & Safety Data Sheet 11.12.1989

## 3. Source of exposure

**Production levels expressed as tons per annum**

1000 - 5000 tons/year (1994)

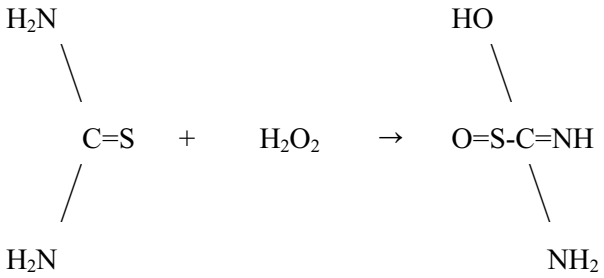
sources of potential human or environmental exposure:
At the Austrian production plant synthesis is performed in a closed batch process.
6 workers can get in contact with product over a time of 4 hours daily. Dust will be exhausted, whenever dust of product occurs, the dust is filtered off and recycled to process.
Concentration of formamidine sulfinic acid in air (mean/day) (production plant Weißenstein):
production, filling in big bags, plant-cleaning: 1,4 mg/m$^3$
production, filling in drums, plant-cleaning: 2,4 mg/m$^3$
production, stock: 0,2 mg/m$^3$
Concentration of formamidine sulfinic acid in waste air (production plant Weißenstein):
< 0,5 mg/m$^3$ with reference to 9361 m$^3$/h waste air

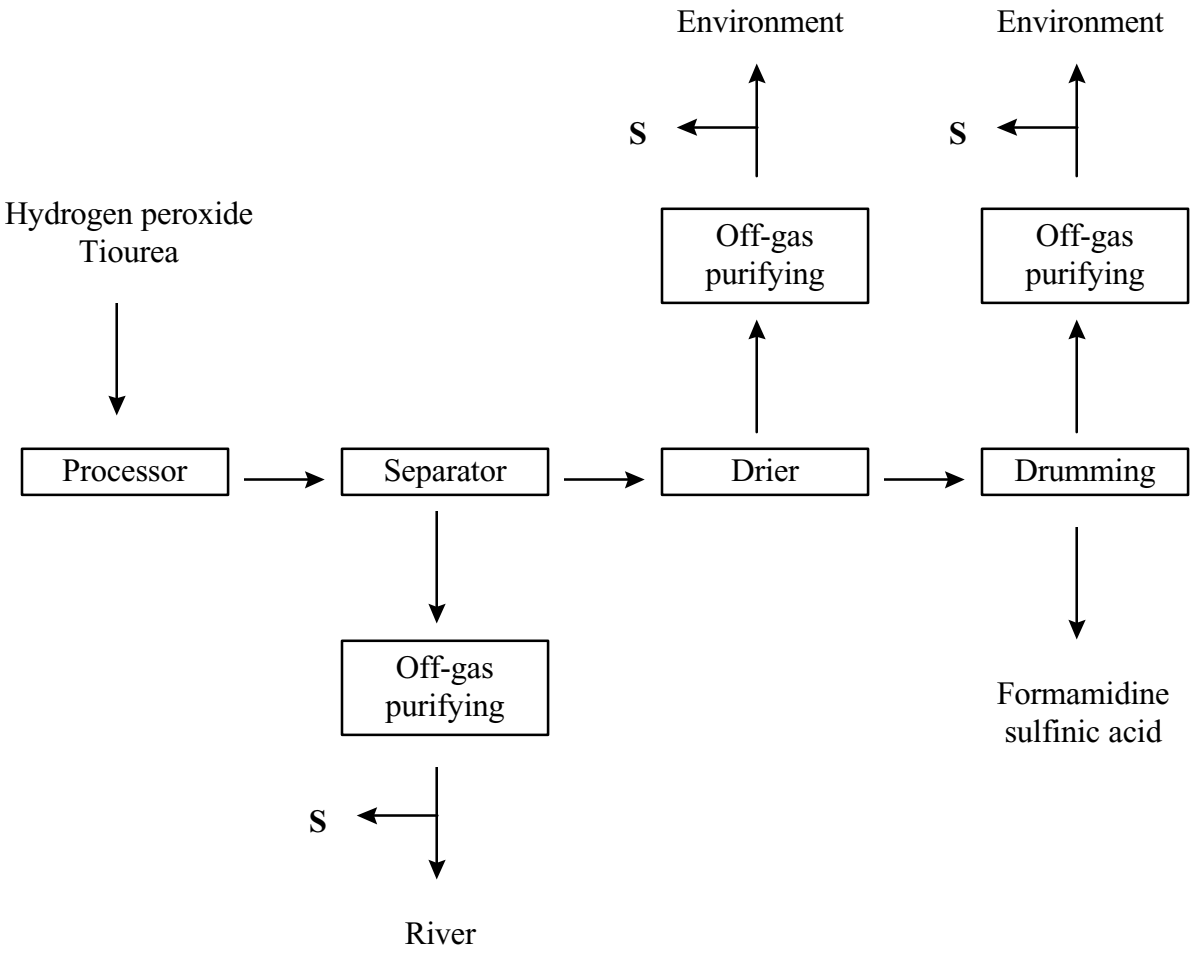
Release to waste water treatment (production plant Weißenstein): 160 - 645 kg/day, product is decomposed by treatment.

Residual product is decomposed during waste water treatment. Off gas is cleaned by filtration and gas washing.

**Production scheme for formamidine sulfinic acid:**

The reaction process for the synthesis of formamidine sulfinic acid is as follows:




**S**: Sampling

Reference: OECW - Degussa Austria Ges.m.b.H.,
A-9721 Weißenstein, IUCLID data sheet 7.8.1995
exposure assessment 2.9.1992
9.8.1996

Dipl.Ing.Dr. D.Wewerka, A-8010 Graz,
report No. 79/93-849 (1993)

österreichische Staub-(Silikose-) Bekämpfungsstelle, Leoben, Austria, report 20.12.1993

**Information concerning Uses**

The product is used in paper recycling, textile printing.
The product is also a component of decolorisation agents.
The product is used in leather processing industry,
paper, pulp and board industry,
photographic industry,
textile processing industry,
bleaching and reducing agents
In Sweden formamidine sulfinic acid is used in one product for the textile industry (240 tons/year 1995).
In Switzerland less than 10 products are in use for decolorising textiles. In all products the concentration of FAS is very high (up to 100%). Most products are for industrial use only. Some are available also for the general customer. The products are in "Giftklasse 3" of the Swiss system corresponding to "toxic, T" in the EC. The trade quantities in Switzerland are assumed to be small.
In France formamidine sulfinic acid is currently not used for production of pulp or paper. It has been used in tests though at an application rate of 0,5%. The decomposition rate was nearly 100%.
In Norway formamidine sulfinic acid is not registered in the Norwegian Product Register.
In the Czech Republic formamidine sulfinic acid is not produced or imported.
In U.S.A. the imported volume of formamidine sulfinic of two from three companies is about 302 tons/y (full information not available)

When the product is used, it reacts to sulphate and urea.
The amount of dust emitted is small, because the product for customer (industrial) use is coarse grained.

**Options for disposal**

Mode of disposal - emptied bags to incineration

Reference: OECW - Degussa Austria Ges.m.b.H.,
A-9721 Weienstein, exposure assessment 2.9.1992
IUCLID data sheet 7.8.1995
Bundesamt für Gesundheit, CH-3003 Bern
Ministry of Environment of Czech Republic, CZ-00 10 Prague 10
Ministry of Environment, F-75302 Paris
National Chemicals Inspectorate
S-17127 Solna Sweden
Norwegian Pollution Control Authority
N-0032 Oslo
U.S. Environmental Protection Agency
Washington, DC 20460, U.S.A.

## 4. Environment

### Biodegradability

Test type: aerobic

Test medium: sewage treatment

Test method: NEN 3235 section 5.4, closed bottle test

GLP YES **[ ]**
NO **[X]**

Test results: concentration formamidine sulfinic acid 2 mg/l
BOD 0,42 mg $O_2$/l after 5-day incubation period (71%)

concentration formamidine sulfinic acid 10mg/l
BOD 1,70 mg $O_2$/l after 5-day incubation period (57%)

Comments: The procedure was carried out in conformity with NEN 3235 section 5.4 (Netherlands Normalisatie Institute NNI, Rijswijk, 1972). The study was not performed under GLP regulations. Formamidine sulfinic acid was tested for bacterial degradability at concentrations of 2,0 and 10,0 mg/l; as microbiotic source an inoculum was obtained from a local municipal sewage treatment plant. After incubation for 5 days in a closed bottle the oxygen consumption was determined (biochemical oxygen demand - BOD). With 2 mg sodium acetate which served as positive control a BOD of 58% of the theoretical oxygen demand was found. With formamidine sulfinic acid the BOD was 71% and 57% for the low and high concentration, respectively. It was concluded that formamidine sulfinic acid appeared not be toxic to the microorganisms in the inoculum. Furthermore the study shows that the test compound is degradable under the conditions of the test.

Reference: Degussa AG, unpublished,
report no.: US-IT-Nr. 89-0019-DKO (1989)

### Chemical Oxygen demand

Test method: NEN 6633,
"Determination of the chemical oxygen demand", Netherlands Normalisatie Institute.
NNI, Rijswijk, October 1987
EEC Directive 84/449, Annex Part C, Methods for the determination of ecotoxicity, C.9:
"Degradation - Chemical oxygen demand", EEC Publication No. L251, September 1984

GLP YES **[X]** US FDA(21 CFR 58),
US EPA (40 CFR 160, 40 CFR 792), OECD
NO **[ ]**

Test results: 0,415g COD/g Formamidine sulfinic acid

Comments: 102,5mg Formamidine sulfinic acid (FAS) was dissolved in 100ml Milli-Ro water. 10ml of this stock solution and 10ml Milli-Ro water were brought into a 250ml round bottom flask. After the addition of anti bumping stones, 2ml sulphuric acid (18 M), 10ml potassium dichromate (0,04 M) and 30ml sulphuric acid, containing silver sulphate, the solution was boiled under reflux for two hours. The remaining potassium dichromate was thereafter titrated, using a freshly normalised ferrous(2)ammonium sulphate (0,104 M) solution and ferroin solution as an indicator. A blank, containing 10ml Milli-Ro water instead of 10ml test substance stock solution, was run simultaneously. The test was performed in triplicate (0,410 g COD/g FAS, 0,415 g COD/g FAS, 0,420 g COD/g FAS)

Reference: RCC NOTOX B.V., NL-5231 DD's-Hertogenbosch,
report no. 1037/C759 (November 1988)

**Stability in air and in water**

Test method or estimation method: Stability of aqueous formamidine sulfinic acid in contact with air

GLP YES **[ ]**
NO **[X]**

Test results: formamidine sulfinic acid is instable under these conditions and the reaction products are acid.

Percentage of degradation after certain period: more than 30%
after 22 hours

Comments: An aqueous solution of 1 g formamidine sulfinic acid/l water was contacted with air (380 ml/min) at 20°C. The pH-value of this solution decreased from a pH of 6,9 to 5,4 after 22 hours. The reference sample shows, that the pH of drinking water (8E dH) increased under the test conditions from 7,1 to 8,5. This is caused by removal of $CO_2$. Therefore the building rate of acid in the formamidine sulfinic acid solution is higher than indicated by the decrease of the pH-value.

Reference: OECW - Degussa Austria Ges.m.b.H.,
A-9721 Weißenstein, Test report Jan. 26, 1994

## 5. Ecotoxicological Data

**Toxicity to fish**

Test species: guppy (Poecilia reticulata)

Test method: OECD GUIDELINE NO.: 203

GLP YES **[X]**
NO **[ ]**

Test results: $LC_{50}$/96 hours: 416 mg/l
NOEC: 180 mg/l

$LC_{50}$ values were calculated from the probits of the percentages of dead fish and the logarithms of the corresponding concentrations using the maximum likelihood estimation method (Finney, D.J., 1971: Probit analysis, Cambridge University Press, Cambridge, UK., 3rd edition)

Comments: Formamidine sulfinic acid was tested in conformity with OECD guideline 203, April 4, 1984. Young guppies of 1-3 cm length were exposed to various concentrations of the test compound for 96 hours. They were not fed for 24 hours prior to test and throughout the test period. Test media were renewed at each 24 hour interval (semistatic procedure). The concentrations tested were 0; 100; 180; 320; 560 and 1000 mg/l; they had been selected on the basis of a preliminary test in which groups of 5 fish were exposed to a range between 0,1 and 1000 mg/l. In the main study after 48 hours 100% mortality was observed at 1000 mg/l; 10% mortality at 560 mg/l and no mortality at lower concentrations. After 96 hours 80% mortality was seen at 560 mg/l and 20% mortality at 320 mg/l. In addition increased pigmentation and decreased swimming ability were recorded at 320 mg/l and higher. The 96-hour-$LC_{50}$ was 416 mg/l, the NOEC was 180 mg/l.

Reference: Degussa AG, unpublished,
report no.: US-IT-Nr.: 88-0049-DGO (1988)

**Toxicity to daphnids**

Test species: Daphnia magna

Test method: OECD GUIDELINE NO.: 202

GLP YES **[X]**
NO **[ ]**

Test results: $EC_{50}$ 390 mg/l
NOEC 180 mg/l

$EC_{50}$ values for the 24 hours exposure period were calculated from the probits of the percentages of affected Daphnia magna and the logarithms of the corresponding concentrations using the maximum likelihood estimation method (Finney, D.J., 1971: Probit analysis, Cambridge University Press, Cambridge, UK., 3rd edition).

Comments: Formamidine sulfinic acid was tested in conformity with OECD guideline 202 of April 4, 1984. Less than 24 hours old Daphnia magna animals were exposed to various concentrations of the test compound for 24 hours. Concentrations tested were selected on the basis of preliminary tests and were between 100 to 1000 mg/l. At least 10 animals were exposed to each concentration. Potassium dichromate was used as a positive control, with which an $EC_{50}$ value between 1,0 and 1,8 mg/l was found. This was in the expected range and confirmed the validity of the test system. Furthermore in the control vessels immobilisation did not exceed 10%. It was found that 100% immobilisation by formamidine sulfinic acid occurred at 1000 mg/l, the No-Observed-Effect-Concentration (NOEC) was 180 mg/l and the $EC_{50}$ was 390 mg/l.

Reference: Degussa AG, unpublished,
report no.: US-IT-Nr.:88-0048-DGO (1988)

**Toxicity to algae**

Test species: Scenedesmus subspicatus

Test method: OECD GUIDELINE NO.: 201

GLP YES **[X]**
NO **[ ]**

Test results: $EC_{50}$ (72 hours) 32,0 mg/l
NOEC (inhibition) 27 mg/l
NOEC (stimulation) 7,5 mg/l

Comments: The effect of formamidine sulfinic acid on growth of the fresh water green algae Scenedesmus subspicatus was studied according to OECD guideline 201, June 7, 1984. The test was performed on exponentially growing cultures of the algae; cell numbers were counted at the beginning of incubation and then after 24, 48 and 72 hours. Potassium dichromate served as a positive control; it was inhibitory on algae growth rate with an $EC_{50}$ of approximately 0,5 mg/l demonstrating the validity of the test system. In a range finding test with formamidine sulfinic acid almost complete inhibition of the algae growth was found between 64,2 and 116,5 mg/l; the $EC_{50}$ was estimated graphically to occur in the range of 25,7 to 64,2 mg/l. Therefore in the main test concentrations in the range between 0 and 64 mg/l were used. HPLC analysis and UV photometry revealed that the compound decomposed over the testing period of 72 hours. Therefore $EC_{50}$ calculations were performed with the nominal test substance concentrations. The main test for effects of formamidine sulfinic acid an algae growth was performed in triplicate. Inhibition of greater 90% was found at 64 mg/l. The $EC_{50}$ was 32,0 mg/l. The No-Observed-Effect

concentration for growth inhibition was 27 mg/l. At lower concentrations there appeared to be a stimulation of growth for which a No-Observed-Effect concentration of 7,5 mg/l was calculated.

Reference: Agrolinz Ges.m.b.H. A-4060 Leonding,
report no. 1136 (July 1992)

**Toxicity to bacteria**

Test species: Pseudomonas putida bacteria

Test method: NEN 6509 (1980)

GLP YES **[X]**
NO **[ ]**

Test results: toxicity threshold value: 538 mg/l

Comments: Formamidine sulfinic acid was evaluated for its ability to inhibit cell multiplication of the bacteria species pseudomonas putida. It was conducted in compliance with GLP regulations. Cultures of the bacteria were exposed to concentrations between 0,5 and 1000 mg test compound/l and were incubated for 18 +/- 2 hours at 25°C. Cell number was estimated by turbidity measurement at 436 nm. Methanol was used as a positive control, and a "toxicity threshold" of 17,7 mg/l was found; it was concluded that the test system was valid. With formamidine sulfinic acid a toxicity threshold value of 538 mg/l was found.

Reference: Degussa AG, unpublished,
report no.: US-IT-Nr.: 88-0044-DGO (1988)

## 6. Toxicological Data

**Acute oral toxicity**

Test species/strain: rat, Sprague-Dawley (S.Ivanovas, Kisslegg/Whrtt.)

Test method: see comments

GLP YES **[ ]**
NO **[X]**

Test results: $LD_{50}$ 1120 mg/kg

Comments: The test was performed before guidelines and GLP regulations were developed. Groups of 5 male and 5 female Sprague Dawley rats each received formamidine sulfinic acid at 5

different doses once orally by gavage. Doses used are not indicated. Signs of intoxication were sedation, ataxia, lying on belly or flank, hypoventilation and reduced reflexes beginning after 6 to 8 hours. Death occured within 18 to 72 hours. After necropsy there was possibly lung edema. The $LD_{50}$ was calculated according to Litchfield and Wilcoxon at 1120 mg/kg. "Toxicity threshold" is reported to be approximately at 900 mg/kg.

Reference: Degussa AG, unpublished,
report no.: US-IT-Nr.: 70-0004-DKT (1970)

**Acute inhalation toxicity**

Test species/strain: rat, Him:OFA, Sprague Dawley, SPF

Test method: OECD GUIDELINE NO.: 403

GLP YES **[X]**
NO **[ ]**

Test results: LC50: 0,164 mg/l/4hours

Comments: Formamidine sulfinic acid was tested according to OECD guideline 403 of May 12, 1981. Groups of 5 male and 5 female Sprague Dawley rats (Him:OFA) each were exposed for 4 hours to air containing 59, 117 and 229 mg formamidine sulfinic acid per $m^3$ air in a nose-only inhalation device. For this purpose a watery solution of the test compound was nebulized; the actual concentrations in the aerosol were determined 9 or 10 times during each inhalation period. In the high concentration group all animals died 1 or 2 days after treatment. In the mid concentration group there was temporary loss of body weights during the first week. Observations in life included ruffled fur, chromodacryorrhea and difficulties in breathing in all mid and high-dosed animals. In the low dose group difficulties in breathing were hardly detected. Anemia and cyanosis as well as low locomotion were found in some mid- and high-dosed animals. At terminal necropsy no lesions were found in 5/10 animals of low-dosed group: in all other animals, haemorrhages or white coverings were found in the lungs, the severity depending on the concentration. Histopathology revealed a corrosive action of test compound in the lung as indicated by multifocal fibrosis, inflammation, proliferation, edema, congestion, loss of cilia etc. Some of these changes were present in the low-dose group and increased with increasing doses. Trachea and nasal cavity were also affected. An $LC_{50}$ of 0,164 mg/l/4 hrs was calculated.

Reference: Österreichisches Forschungszentrum Seibersdorf,
A-2444 Seibersdorf (September 1992)

**Acute dermal toxicity**

Test species/strain: rat, Him:OFA, Sprague Dawley, SPF

Test method: OECD GUIDELINE NO.: 402

GLP YES **[X]**
NO **[ ]**

Test results: $LD_{50}$ > 2000 mg/kg

Comments: Formamidine sulfinic acid was tested according to OECD guideline 402, February 24, 1987. 5 male and 5 female Sprague Dawley rats (Him:OFA) were hair-clipped and received 1 day later a dermal dose of 2000 mg formamidine sulfinic acid/kg body weight. Application was achieved by spreading the test substance over an area of approx. 5 x 6 cm and moistening with destilled water. The area was then covered by a cellulose patch for 24 hours. The only adverse in-life-observation was chromodacryorrhea which occurred maximally 1 day after administration of the compound in all males and 4/5 females. This was attributed to reduced well-being caused by the dressing. At necropsy no changes were observed that could unequivocally be attributed to the test compound. It is concluded that the $LD_{50}$ (dermal) of formamidine sulfinic acid is beyond 2000 mg/kg b.w.

Reference: Österreichisches Forschungszentrum Seibersdorf, A-2444 Seibersdorf (March 1992)

**Skin Irritation**

Test species/strain: albino rabbit, New Zealand white

Test method: patch-test on the abraded and intact skin

GLP YES **[ ]**
NO **[X]**

Test results: give maximum scores after 72 hrs
4 erythema intact skin
2 edema
average 3.3
4 erythema abraded skin
2 edema
average 5.3

Comments: The test was performed in 1981. 12 New Zealand white rabbits were hair-clipped and in 6 of them the skin was abraded. 0,5 g of the test compound (a 40% mixture with water) was brought on the intact or abraded skin under a surgical patch of 1 inch x 1 inch which was left in place for 24 hours. At this time and 48 hours later lesions were evaluated according to Draize or to an institute-own grading system. At both time points it was found that formamidine sulfinic acid was moderately irritating to the intact skin and severely irritating to the abraded skin.

Reference: TNO, NL-3700 AJ Zeist, project no. B81-0061-35

**Eye Irritation**

Test species/strain: albino rabbit, New Zealand white

Test method: FDA (Fed. Reg. 28 (119),5582, 1963)
Draize, Kelley
(Drug Cosmet. Industr. 71 (1952) 36)

GLP YES **[ ]**
NO **[X]**

Test results: give maximum scores after 7 days:
2-3 cornea
1 iris
1 conjunctivae redness
2 conjunctivae chemosis

Comments: Formamidine sulfinic acid was tested for eye irritation according to procedures published by the FDA (1963) and Draize and Kelley (1952). 6 New Zealand white rabbits received a treatment with 100 mg of the test compound on the everted lower lid of one eye. After 24 hours slight opacity of the cornea, slight iritis and moderate redness and slight to severe swelling of the conjunctivae were noted. In the course of the 7 day observation period some of these effects recovered partly or completely. However, at 7 days slight to severe cornea opacity and vascularization of the cornea were observed in 4 rabbits, ulcus cornea in 2 rabbits, slight iritis in 3 rabbits and slight lesions of the conjunctivae in all rabbits. It was concluded that according to the FDA standards formamidine sulfinic acid was a severe eye irritant.

Reference: TNO, NL-3700 AJ Zeist, report no. V 81.353/210061

**Skin sensitisation**

Test species/strain: guinea pig

Test method: see comments

GLP YES **[ ]**
NO **[X]**

Test results: Number of animals with skin reaction at challenge: 0

Comments: Formamidine sulfinic acid was injected daily for 10 days intracutaneously into the hair-clipped skin of guinea pigs. The strain of guinea pigs used had previously been shown to be responsive to sensitisation by 2,4-dinitrochlorobenzene. The doses of the test compound injected were selected to produce no local reactions, and the place of injection was altered daily. After

further 10 days without treatment the test compound was again injected intracutaneously on 2 subsequent days, and 24 and 48 hours later local reactions were registered. There were no reactions observed exceeding those of physiological saline which served as negative control. It was concluded that formamidine sulfinic acid had no sensitising effect under the conditions of the present study.

Reference: Degussa AG, unpublished,
report no.: US-IT-Nr.: 70-0003-DKT (1970)

**Repeated dose toxicity**

Test species/strain: rat, Wistar, CRL:(WI)BR

Test method: OECD GUIDELINE NO.: 407

GLP YES **[X]**
NO **[ ]**

Test results: Dose or concentration at which no toxic effects were observed:
47 mg/kg b.w.

Comments: Formamidine sulfinic acid was tested according to OECD guideline 407 of May 12,1981. Groups of 5 male and 5 female Wistar rats each received once per day on 5 days per week during 4 consecutive weeks an oral dose of the test compound per gavage. Doses were 0, 15, 47 and 150 mg/kg body weight per day. These doses were selected on the basis of a preliminary study in which 80, 240 or 720 mg test compound/kg b.w. had been administered to rats for 7 consecutive days. In this preliminary study the high dose caused death of 9/10 animals and 240 mg/kg caused significant loss of body weight, lower food consumption and thymus atrophy in all animals. In the main study no deaths occurred. Changes observed in the high dose group (150 mg/kg) included reduced body weight gain, reduced food consumption, raised fur, reduction of serum levels of cholesterol, glucose and alkaline phosphatase, elevation of serum levels of bilirubin and inorganic phosphate, reduced weights of the thymus. In the mid dose group only a decrease of serum alkaline phosphatase was found. Histopathological analysis did not reveal unequivocally substance related effects. Since the decreased alkaline phosphatase at the mid dose level was an isolated effect it was concluded that the No-Adverse-Effect-Level was 47 mg formamidine sulfinic acid per kg body weight in both sexes of rats.

Reference: Österreichisches Forschungszentrum Seibersdorf,
A-2444 Seibersdorf (July 1992)

**Bacterial test**

Test species/strain: Salmonella typhimurium/TA 1535, TA 1537, TA 1538, TA 98, TA 100

Escherichia coli/WP2 uvrA$^-$ (pKM101)

Test method: Ames test

GLP YES **[ ]**
NO **[X]**

Test results: Minimum concentration of test substance at which toxicity to bacteria was observed:
with metabolic activation: 5 mg/plate
without metabolic activation: 5 mg/plate

Genotoxic effects:

| | + | ? | - |
|---|---|---|---|
| with metabolic activation: | **[X]** | **[ ]** | **[ ]** |
| without metabolic activation: | **[X]** | **[ ]** | **[ ]** |

Comments: Test performance was similar to OECD guideline 471. The specific tests performed were not subjected to inspection for quality assurance although the processes involved were inspected at predetermined intervals. The report was audited by IRI quality assurance personal according to SOP. Formamidine sulfinic acid was tested for mutagenic activity in an Ames test using Salmonella typhimurium strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100 and Escherichia coli strain WP2 uvrA$^-$ (pKM101). All tests were performed with and without metabolic activation system (S 9 mix from arochlor-treated male Sprague Dawley rats). Adequate positive and negative controls were used in some but not all tests performed and where studied showed the validity of the test system. Formamidine sulfinic acid was tested in concentrations of 33,3; 100; 333,3; 1000; 3300 and 10000 g /plate. In a second series of experiments 0,75; 1; 2,5; 5; 7,5 and 10 mg/plate were used. At 1000 and more g/plate the test compound was not completely dissolved. 5 mg/plate and more produced bacterial toxicity. It was found that formamidine sulfinic acid was weakly mutagenic to strain TA 1535 and TA 100 suggesting base-pair substitution mutations. Mutagenicity was detected in the presence and absence of S 9 mix and the lowest concentration causing a mutagenic effect was 0,75 mg/plate.

Reference: Inveresk Research International, EH21 7UB
Musselburgh Scotland, IRI project no. 705022
(July 1981)

**Mammalian cell gene mutation test**

Test species/strain: chinese hamster ovary (CHO) cells
(ATCC: CCL 61)

Test method: OECD GUIDELINE NO.: 476

GLP YES **[X]**
NO **[ ]**

Test results: Minimum concentration of test substance at which toxicity to cells was observed:
with metabolic activation: 800 mg/l
without metabolic activation: 400 mg/l

Genotoxic effects:

| | + | ? | - |
|---|---|---|---|
| with metabolic activation: | **[ ]** | **[ ]** | **[X]** |
| without metabolic activation: | **[ ]** | **[ ]** | **[X]** |

Comments: Formamidine sulfinic acid was tested according to OECD guideline 476 of April 4, 1984, Chinese hamster ovary (CHO) cells were treated with formamidine sulfinic acid in the absence and presence of an exogenous metabolizing system (S 9 mix from arochlor-treated rats). Formation of mutations in the HGPRT-locus were checked by the ability to form colonies in selection medium containing 6-thioguanine. The validity of the test system was confirmed by positive and negative controls. Concentrations of the test compound used were between 50 and 800 mg/l; two independent experiments were performed. At concentrations exceeding 400 mg/l cytotoxicity was observed in the absence of exogenous metabolizing system. At none of the concentrations tested a clear increase of mutant colonies was obtained. It was concluded that formamidine sulfinic acid was not mutagenic in the present test system.

Reference: Österreichisches Forschungszentrum Seibersdorf, A-2444 Seibersdorf (December 1992)

**Non-bacterial test <u>in</u> <u>vivo</u>**

Test species/strain: mouse "NMRI" KFM (outbred, SPF)

Test method: Schmid W., The micronucleus test, Mutation Res.31:9-15, 1975

GLP: YES **[X]** (Fed.Reg.Vol.34,No.247, 22.12.1978,
NO **[ ]** p.60013-60025,USA)

Effect on Mitotic Index or P/N Ratio: 2,5/1,6 high dose

Genotoxic effects:

| + | ? | - |
|---|---|---|
| **[ ]** | **[ ]** | **[X]** |

Comments: formamidine sulfinic acid was tested for its ability to induce micronucleus formation in mouse bone marrow cells. GLP regulations of December 1978, USA, were followed. The testing procedure used was published by W. Schmid. Dose selection was based on a preceding $LD_{50}$

determination according to interagency regulatory guidelines of January 1981 where an $LD_{50}$ of 1486 mg/kg b.w. had been found. In the present assay 5 NMRI mice of each sex were treated per os once daily on 2 consecutive days with either 29,7 or 148,6 or 743,0 mg/kg each, or with solvent (negative control) or with 50 mg cyclophosphamide/kg b.w. (positive control). The group size in the negative control group was 8 animals per sex. The animals were sacrificed 24 hours after the last treatment; no other sacrifice times were investigated. The test compound did not change the ratio of polychromatic to normochromatic erythrocytes in contrast to the positive control. The positive control compound also produced a strong increase in the number of micronuclei demonstrating the validity of the test system. Formamidine sulfinic acid produced a slight dose dependent increase in the number of micronuclei (approximate doubling in polychromatic erythrocytes in the high dose group compared to negative control; positive control showed a 20fold increase). Increases in the test compound treated animals were not statistically significant. Increases in micronuclei of normochromatic cells were significant in males (medium dose) and in females (high dose). However the micronucleus values found were within the range of historical negative control data of the laboratory. It was concluded that the slight increases observed were not test compound related and that the present assay did not reveal chromosome breaking activity or damage to the mitotic apparatus by formamidine sulfinic acid.

Reference: Research & Consulting Company Ltd.,
CH-4452 Itingen, project no. 007244 (April 1982)

**Non-bacterial test <u>in</u> <u>vivo</u>**

Test species/strain: mouse, CD-1
(Supplier: Charles River UK Ltd)

Test method: OECD Guideline No. 474,

GLP: YES **[X]**
NO **[ ]**

Test results: formamidine sulfinic acid does not produce micronuclei in polychromatic erythrocytes under the test conditions
Lowest dose producing toxicity: LD50 799,6 mg/kg

Effect on Mitotic Index or P/N Ratio: 0,94 (72h, male)
0,71 (72h, female)

| Genotoxic effects: | + | ? | - |
|---|---|---|---|
| | **[ ]** | **[ ]** | **[X]** |

Comments: Formamidine sulfinic acid was tested in CD-1 mice for micronucleus induction in bone marrow. OECD test guideline No. 474 was followed. The test compound was dissolved in physiological saline and administered intraperitoneally. Doses were 140, 280 and 560 mg/kg given

once to groups of 5 male and 5 female mice each killed 24, 48 and 72 hours later. Only mice treated with the top dose were evaluated; this dose correspond to approx. 70% of the $LD_{50}$ as judged from a preliminary dose range finding experiment. 3 negative control groups received saline i.p. Positive controls were treated with 40 mg/kg cyclophosphamide (CPA) dissolved in water and administered i.p.; sacrifice was after 24 hours. CPA treatment produced a statistically significant increase in numbers of micronucleated polychromatic erythrocytes. Mice treated with the test compound exhibited decreased ratios of polychromatic to normochromatic erythrocytes; none of these groups showed a statistically significant increase of micronucleated erythrocytes although after 24 and 72 hours numbers were approx. doubled (but still in the range of historical control data). There was a considerable intra-group variation of individual micronucleus counts. The authors concluded that the test compound was not able to induce micronuclei in polychromatic erythrocytes of mouse bone marrow.

Reference: Microtest Research Limited, Y01 5 DU York,
United Kingdom; Report Ref: 31MRESTO.005 (1989)

**Non-bacterial test in vivo**

Test species/strain: mouse, Crl: NMRI BR
(Supplier: Charles River WIGA GmbH)

Test method: OECD Guideline No. 474,
EC Guideline 92/69, Part B.12

GLP: YES **[X]**
NO **[ ]**

Test results: formamidine sulfinic acid does produce micronuclei in polychromatic erythrocytes under the test conditions

Lowest dose producing toxicity:
794 mg/kg b.w. - a marked cytotoxic effect was noted at this dose
500 mg/kg b.w. - slight cytotoxicity, which did not impede the evaluation

Effect on Mitotic Index or P/N Ratio: 5,8/1,2

| Genotoxic effects: | + | ? | - |
|---|---|---|---|
| | **[X]** | **[ ]** | **[ ]** |

Comments: the dose of formamidine sulfinic acid was derived from a preliminary range finding study with male and female NMRI-mice. Doses of 500, 794, 1260 and 2000 mg/kg body weight, respectively, were applied to two males and two females each. At a dose of 2000 mg/kg both females and 1/2 males died within maximum 72 h p.a. At a dose of 1260 mg/kg 1/2 males and 1/2 females died within 48 h p.a. At doses of 794 and 500 mg/kg respectively, all animals survived until 72 h p.a. A marked cytotoxic effect was noted at a dose of 794 mg/kg. Slight cytotoxicity,

which did not impede the evaluation, was observed at a dose of 500 mg/kg. Therefore a dose of 600 mg formamidine sulfinic acid per kg body weight was chosen for the main study. Three groups (5 mice male/group and 5 mice female/group) were treated orally with 600 mg/kg b.w. formamidin sulfinic acid. Three groups (5 mice male/group and 5 mice female/group) were treated orally with 20 ml/kg b.w. 0,5% carboxymethylcellulose in distilled water (negative control). One group (5 mice male/group and 5 mice female/group) was treated orally with 40 ml/kg b.w. Cyclophosphamide dissolved in distilled water (positive control). Animals were killed by cervical dislocation 24, 48 and 72 hours p.a. Bone marrow was obtained from both femurs and prepared according to the method of W. Schmid (the micronucleus test for cytogenetic analyses). For each animal three smears were prepared. Two of them were stained using a slightly modified Pappenheim method, coded and scored. The amount of nucleated cells was decreased in dosed animals 24, 48 and 72 hours p.a. as compared to the appropriate negative control groups and also compared to historical control data, indicating a cytotoxic effect of the test substance at the dose used. In all dosed groups the amount of polychromatic erythrocytes was lowered compared to the respective negative control groups. As all values are still within the range of historical negative controls, this is not regarded as biologically meaningful. There was no significant difference in the rate of micronucleated normochromatic erythrocytes between the dosed groups and the negative control groups. Micronuclei rates of the polychromatic erythrocytes increased from 1,2/1000 (identical at the 3 sampling times) to 5,6/1000, 5,9/1000 and 5,7/1000; positive control 14,5/1000. These increases were statistically significant. Upon re-evaluation of the individual slides by external experts the results were not completely reproducible. It was therefore suggested to repeat the study (letter of Prof.Dr.D.Kayser, BGVV Berlin, 13.3.1995). In conclusion formamidine sulfinic acid had a moderate or weak enhancing effect in micronucleus formation in the bone marrow after oral administration of toxic doses in mice, but it was recommended by external experts to repeat the study.

Reference: Österreichisches Forschungszentrum Seibersdorf, A-2444 Seibersdorf, (June 1994)

**Non-bacterial test <u>in</u> <u>vivo</u>**

Test species/strain: mouse, NMRI BRL (CH-4414 Füllinsdorf)

Test method: OECD Guideline No. 474,
EC Guideline 92/69, Part B.12

GLP: YES **[X]**
NO **[ ]**

Test results: During the study described and under the experimental conditions reported, formamidine sulfinic acid did not induce micronuclei as determined by the micronucleus test with bone marrow cells of the mouse. Therefore, formamidine sulfinic acid is considered to be non-mutagenic in this micronucleus assay.

The text was performed by RCC, Cytotest Cell Research, Roßdorf, Germany, with consultantship by Prof. H.G. Miltenburger.

Lowest dose producing toxicity: 600 mg/kg b.w.

Effect on Mitotic Index or P/N Ratio:

| dose mg/kg b.w. | sampling time | PCEs with micronuclei | range | PCE/NCE |
|---|---|---|---|---|
| 600 | 24 h | 0,12 % | 0 - 3 | 1000/881 |
| 600 | 48 h | 0,11 % | 0 - 3 | 1000/889 |
| 600 | 72 h | 0,11 % | 0 - 3 | 1000/839 |

| Genotoxic effects: | + | ? | - |
|---|---|---|---|
| | [ ] | [ ] | [X] |

Comments: Formamidine sulfinic acid was assessed in the micronucleus assay for its possible potential to induce micronuclei in polychromatic erythrocytes (PCE) in the bone marrow of the mouse with a dose of 600 mg/kg b.w. (at 24 h, 48 h and 72 h preparation interval). 600 mg/kg b.w. formamidine sulfinic acid was estimated by pre-experiments to be the maximum attainable dose. The animals expressed slight toxic reactions.
The mean number of normochromatic erythrocytes was not increased after treatment with formamidine sulfinic acid as compared to the mean values of NCEs of the negative control, indicating that formamidine sulfinic acid had no cytotoxic properties in the bone marrow.
There was no enhancement in the frequency of the detected micronuclei in comparison to the negative control at any preparation interval after administration of formamidine sulfinic acid.
30 mg/kg b.w. cyclophosphamide administered per os was used as positive control which showed a statistically significant increase of induced micronucleus frequency.

Reference: Degussa AG, unpublished,
report no.: US-IT-Nr.: 95-0048-DGM (1995)

**Reproductive toxicity**

Test species/strain: rat, Wistar, CRL:(WI)BR

Test method: OECD GUIDELINE NO.: 421 (final draft) preliminary reproduction screening test

GLP: YES **[X]**
NO **[ ]**

Test results: NOEL for P generation: 47 mg/kg
NOEL for F1 generation: 15 mg/kg

NOEL for F2 generation: ----------

Maternal toxicity: lower mean number of corpora lutea per dam, lower mean total litter size per dam at birth.

Comments: This study was performed as a screening test to evaluate adverse effects on reproductive performance associated with repeated administration of formamidine sulfinic acid, according to OECD guideline 421 (final draft). Formamidine sulfinic acid was administered orally by gavage to 3 groups (low dose, mid dose, high dose) of 12 male and 12 female Wistar rats each once a day. An equally sized negative control group was treated with the vehicle. The test substance was administered freshly dissolved in distilled water at a dose volume of 10 ml per kg body weight. Doses of 0 (control), 15 (low dose), 47 (mid dose) and 150 mg (high dose) test substance per kg body weight and day were used up to day 11 and were reduced to 5 (low dose), 15 (mid dose) and 47 (high dose) mg/kg thereafter due to severe test substance effects. Mating was performed on an 1:1 base after 2 weeks of premating period. Couples were separated after successful mating resp. at the end of 10-days mating period. Dams were allowed to litter normally and were sacrificed together with their offspring on day 4 of lactation. Dosing was started at beginning of pre-mating period and continued until termination of the study.

Investigations performed:
Parental animals: Observations in life; body weight; feed consumption; mating results; time of parturition; necropsy; organ weight analysis; histopathology of selected tissues. Offspring: Observation in life; litter weight; number; sex and viability; necropsy.
The test substance caused severe systemic toxic changes in the high dosed animals at a dose of 150 mg/kg body weight (lower mean body weight, body weight loss, reduced feed consumption, signs of reduced well-being like emaciation, yellow and reduced faeces). After reduction of all doses to a third of the initial doses from day 12 on the animals of the high dose group slowly recovered from most adverse effects, but not from all (e.g. significantly lower body weight). No toxic signs were observed in the low and mid dose group, neither before dose reduction nor thereafter. No treatment related histopathological changes or gross changes were found.
Concerning toxic effects of the test substance, the No-Observed-Adverse-Effect-level in this study for both sexes is therefore considered to be 47 mg formamidine sulfinic acid per kg body weight, when administered daily on seven days per week.

Parameters of fertility like time until conception, duration of pregnancy or fertility index were unaffected by treatment with the test substance. Significant effects of the test substance on reproduction were a lower mean number of corpora lutea per dam and a lower mean total litter size per dam at birth in the high dose group, compared to the negative control group. These effects are probably caused by maternal toxicity at the initial high dose of 150 mg/kg. Nevertheless, adverse effects on reproduction cannot be excluded at the reduced high dose of 47 mg/kg, Therefore the No-Observed-Adverse-Level for reproductive performance is considered to be 15 mg formamidine sulfinic acid per kg body weight under the conditions of this study.

Reference: Österreichisches Forschungszentrum Seibersdorf,

A-2444 Seibersdorf, (June 1993)

## 7. Experience with Human Exposure

Concerning the use of Methanesulfinic acid deriv. in consumer products in Germany there is no exposure data available.

Reference: Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, D-44061 Dortmund
letter from 10.01.1997

In 85 persons of a production plant no increased frequency of formamidine sulfinic acid related symptoms was observed after 2 years

Reference: OECW - Degussa Austria Ges.m.b.H.,
A-9721 Weißenstein, IUCLID Data Sheet 7.8.1995

## 8. Initial Assessment

Formamidine sulfinic acid (FAS) is a white powder which is soluble in water (max. 27 g/l). It decomposes upon heating > 50°C and spontaneously beyond 100°C (exotherm) under formation of SO2. The partition coefficient octanol/water is low: log $P_{OW}$ -3,23. Also the vapour pressure is low: < 0,36 Pa at 30°C.

FAS is manufactured at a single plant in Austria. Production levels reported are 1000-5000 t/year. Production of FAS in other countries is not known. FAS is manufactured mainly for industrial purposes. It is a strong reductant and is used to discolorate dyes in paper recycling, textile printing and similar processes. When used the product decomposes to sulphate and urea.

Human Health

Human exposure: Exposure may occur at the workplace, mainly by inhalation of FAS dust. At the Austrian production plant 6 workers can be exposed to 0,2-2,4 mg FAS dust/$m^3$ (mean/shift). Exposure at work places of industrial users is expected to be low, because the product for customer use is coarse grained to reduce dust emissions. Due to the low vapour pressure no relevant exposure to FAS vapour is to be expected. There is no known direct exposure of the general consumer except in Switzerland, where FAS is on market in small quantities.

Potential indirect exposure was modelled by means of the USES V 1.0 NL program; a total human dose of 2,153 x $10^{-7}$ mg/kg daily was calculated.

Health effects: Aqueous aerosols of FAS were very toxic upon acute inhalation ($LC_{50}$ 0,164 mg/l/4 h in rats); at histopathological examination lung, nasal cavity and trachea showed inflammation,

haemorrhage, edema, fibrosis in all treated groups. including the low dose group (59 mg/$m^3$ air). No repeated dose inhalation study is available in the SIDS. Acute oral toxicity of FAS is low ($LD_{50}$ 1120 mg/kg in rats). Repeated oral application of FAS to rats for 4 weeks on 5 days/week revealed a NOEL of 47 mg/kg. Higher doses produced various signs of intoxication, but no organ-specific histopathological effects were noted. There was no acute dermal toxicity ($LD_{50}$ > 2000 mg/kg in rats). FAS was moderately irritating to the intact skin and severely irritating to the abraded skin and to eyes in rabbits. There was no evidence of skin sensitisation in guinea pigs.

Studies on genetic toxicity showed a weakly mutagenic effect in Salmonella strains TA 1535 and TA 100 with and without metabolic activation (the study was reported in 1981 and did not conform to OECD guidelines and GLP regulation). No mutagenic activity of FAS was detected in a mammalian cell system (CHO cells with and without metabolic activation) which was performed according to current OECD guidelines under GLP rule. Of 4 micronucleus tests performed with FAS in vivo in mouse bone marrow one single test was weakly positive but the validity of this study was questioned. It was concluded that the weight of evidence clearly supported non-mutagenicity of FAS in mouse bone marrow in vivo. Adverse effects on reproduction of rats were found after doses of 150 mg/kg changed to 47 mg/kg after 11 days of treatment, i.e. 3 days before mating because of maternal toxicity at 150 mg/kg. Adverse effects were lower mean number of corpora lutea/dam and lower mean total litter size/dam at birth. No maternal or reproductive toxicity was noted to 5 mg/kg on day 12. Although it could not be excluded that reproductive toxicity seen after 150/47 mg/kg was due to the initial high dose, the NOEL was considered to be 15 mg/kg.

No documented effects of FAS on human health are known to us.

In conclusion FAS appears of little concern to human health provided that workers are appropriately protected from inhalation of FAS dust and from $SO_2$ forming during thermal decomposition. In Switzerland products available to the general consumer are labelled as "Giftklasse 2" corresponding to "toxic". The margins of safety for humans were calculated by modelling to be 9.000 locally and 2 x $10^8$ regionally.

Environment

Exposure: Release to waste water treatment plant at the production site is between 160 and 645 kg FAS/day; measured data on release at customer plants into waste water are not available. When the product is used, it degrades to sulfate and urea. FAS decomposes in water (> 30% in 22 h) and is biodegradable. It is not toxic to bacteria. Because of its low partition coefficient octanol/water no potential for bioaccumulation is expected.

Discharge into air at the production site is < 1 mg FAS/$m^3$ and < 0,5 kg/day. Discharge of FAS dust from plants where FAS is expected to be small, because the product is coarse grained.

Environmental distribution and exposure have been modelled using the USES V 1.0 NL program. Daily local emissions from STP into air were calculated to be 0,18, to water 9,2, to suspended matter 3,4 x $10^{-8}$ and to sludge 8 x $10^{-6}$, all in kg.

Effects: FAS is of low aqua-toxicity. With fish (Poecilia reticulata) an $LC_{50}$/96 h value of 416 mg/l was found in a semistatic procedure, at 48 h toxicity was lower ($LC_{50}$ approx 700 mg/l). Immobilisation of Daphnia magna occurred with an $EC_{50}$ of 390 mg/l. Growth inhibition of the alga Scenedesmus subspicatus was obtained with an $EC_{50}$ (72 h) of 32 mg/l. Below 27 mg/l a stimulation of growth was seen, and a NOEC of 7,5 mg/l (including the stimulatory effect) was calculated. Inhibition of multiplication of bacterium Pseudomonas putida was found beyond a "toxicity threshold" value of 538 mg/l.

In conclusion, because of low bioaccumulation potential, limited stability in water, low levels of exposure and a low toxicity to aquatic organisms this chemical shows low environmental concern. The probability for PEC/NEC > 1 is 0,2858.

## 9. Conclusions and recommendations

FAS is mainly used for industrial purposes and no direct exposure of the general consumer is expected in most countries. Inhaled aqueous aerosols of FAS were highly toxic to rats. Therefore, adequate protection of workers and customers from inhalation of FAS is required at the work place. Estimated exposures of workers at the Austrian production site are lower (at least 25fold) than toxic doses in animals. Exposures are expected to be even lower at work places of industrial customers. No potential human health risks are envisaged provided that appropriate measures to protect from inhalation of dust are taken at the work place. In countries where general consumers have access to FAS appropriate labelling of the product as "very toxic" at inhalation should be required. Due to its limited stability, extremely low $P_{OW}$, low toxicity to water organisms, low environmental exposure and a calculated PEC/NEC ratio > 1 FAS does not appear to be of significant environmental concern.

It is recommended that adequate protective measures are taken. No further testing of FAS is required as long as its use pattern and the exposure situation remain unchanged.