

# **Final HPV Assessment Report**

**on**

**Methanesulfonic acid**

**CAS No. 75-75-2**

**Submitted by: Arkema Inc.**

**May 20, 2008**

Atofina Chemicals, Inc. and Chevron Phillips Chemical Company LP formed a consortium<sup>1</sup> under the auspices of the Mercaptan Thiol Council (MTC) to participate in the United States High Production Volume (HPV) Chemical Challenge Program for methanesulfonic acid (CAS No. 75-75-2). The consortium submitted a proposed test plan and robust summary to EPA on January 10, 2003. EPA posted the submission on the ChemRTK HPV Challenge Website on February 5, 2003. EPA reviewed this submission and provided comments to the sponsors on June 17, 2003. The sponsors submitted a revised test plan to EPA on August 23, 2003. We have now completed the testing and have updated the robust summary. This assessment report and the revised robust summary constitute the final submission to fulfil our commitment to supply information for methanesulfonic acid under the HPV program.

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<sup>1</sup> Chevron-Phillips ceased manufacturing methanesulfonic acid and withdrew from the consortium in 2007. Atofina changed to the current name of Arkema Inc. in 2005.

## 1.0. Uses and sources of exposure

Methanesulfonic acid is available in commercial quantities as a 70% solution in water and in anhydrous form. It is used in acid catalysts, chemical manufacturing and extraction, health and pharmaceutical, leather and textile processing and metalworking and metal process. The majority of the applications are industrial in nature, and MSA is reacted and consumed in these processes. Potential industrial worker exposure is limited to use in spray up applications and transfer from small packages in which they are shipped to charge tank, reactor or mixing vessel.

## 2.0. Evaluation of HPV data endpoints

### 2.1. Physico-chemical properties

|  | Value              | Reference       |
|--|--------------------|-----------------|
| Melting point                                | 19°C               | Atofina (1993)  |
| Boiling point                                | 167 °C at 13 hPa   | Budavari (1989) |
| Vapor pressure                               | 0.013 hPa at 20 °C | Atofina (1993)  |
| Water solubility                             | 1000 g/L at 20 °C  | Lewis (1993)    |
| Partition coefficient (log K <sub>ow</sub> ) | -4.98              | Leo (1978)      |
| Dissociation constant (pKa)                  | -1.86              | Serjeant (1979) |

### 2.2. Environmental fate

#### 2.2.1. Photodegradation

MSA in air is not expected to undergo direct photolysis, but may undergo indirect photolysis through hydroxyl radical oxidation. The hydroxyl radical reaction was calculated using AOPWIN® version 1.90 (EPIWIN v.3.1). The overall hydroxyl radical reaction rate constant is  $0.276 \times 10^{-12}$  cm<sup>3</sup>/molecule-sec, with an estimated half-life of 38.8 days.

#### 2.2.2. Stability in water (Hydrolysis)

MSA is a stable strong organic acid. As such, it readily protonates water to form hydronium ions (e.g., H<sub>3</sub>O<sup>+</sup>, H<sub>7</sub>O<sub>3</sub><sup>+</sup>) and methanesulfonate anion (CH<sub>3</sub>SO<sub>3</sub><sup>-</sup>). No further degradation of methanesulfonate anion occurs in pure water. The shelf life of 70% aqueous solution MSA was tested by storing two unopened drums under normal ambient conditions (temperature ranged from -10°C to +30°C) for 24 months. No appreciable degradation was observed. These results demonstrate that MSA is hydrolytically stable.

In their comment on our test plan for MSA, EPA agreed with the submitter's technical discussion and considered this endpoint fulfilled.

#### 2.2.3. Biodegradability

MSA (70% in water) attained 100% degradation within 28 days in an OECD 301A DOC Die Away Test such that it can be considered as readily biodegradable (Elf Atochem, 1995). In an OECD 303A Sewage Treatment Coupled Unit Simulation Test, the mean biodegradation percentage of MSA (purity not specified) was 86.6% from day 55 to day 68 (SNEAP, 1989).

#### **2.2.4. Distribution in environmental matrices**

The EQC Level III Fugacity model was used to evaluate the fate, transport and distribution of MSA between environmental matrices. Using loading rates of 1000 kg/h each for air, soil and water, it predicts the following percent distribution when it is released simultaneously to all three compartments: Air = 0.4%; Soil = 54.0%; Water = 45.6%; Sediment = 0.07% (EPIWIN 3.1).

### **2.3. Ecotoxicity**

#### **2.3.1. Acute toxicity to fish**

In an OECD 203 study, groups of ten fish (*Oncorhynchus mykiss*) were exposed for 96 hours to nominal concentrations of MSA (70.3% in water) of 0 (control), 13, 22, 37, 60 and 100 mg/L (Elf Atochem, 1998a). In an effort to evaluate the effect of pH on the toxicity of the test substance to the exposed organisms, a duplicate set of test solutions was established at the 60 and 100 mg/L treatment levels. The pH of these solutions was adjusted to 7.1 - 7.3 with sodium hydroxide. There was 100% mortality at 100 mg/L. The 96-hour LC<sub>50</sub> was 73 mg/L. The No-Observed-Effect Concentration (NOEC) was determined to be 56 mg/L. No mortality was noted in the solutions that were adjusted to pH 7.1 to 7.3.

#### **2.3.2. Acute toxicity to daphnids**

In an OECD 202 study, groups of five daphnids (*Daphnia magna*) were exposed for 48 hours to nominal MSA (70.3% in water) concentrations of 0 (control), 120, 210, 330, 570 and 890 mg/L (Elf Atochem, 1998b). In an effort to evaluate the effect of pH on the toxicity of the test substance to the exposed organisms, a duplicate set of exposure solutions was established at 620 and 900 mg/L. Based on measured concentrations, the 48-hour EC<sub>50</sub> value was 260 mg/L. The NOEC through 48 hours was 120 mg/L. Immobilization in the 620 and 900 mg/L solutions that were adjusted to pH 7.9 to 8.3 were similar to that of the control. These data indicate that the acidic nature of the non-pH adjusted test solution probably contributed to the immobilization observed during the definitive test.

#### **2.3.3. Acute toxicity to algae**

In an OECD 201 study, algae (*Selenastrum capricornutum*) were exposed for 72 hours to nominal MSA (70.3% in water) concentrations of 0 (control), 3.1, 6.3, 13, 25, 50, and 100 mg/L (Elf Atochem, 1998c). In an effort to evaluate the effect of pH on the toxicity of the test substance to the exposed organisms, a duplicate set of exposure solutions was established at 50 and 100 mg/L adjusted to pH 7.5. Measured concentrations were at least 87% of nominal concentrations. Based on cell density, the NOEC was determined to be 5.8 mg/L. The 96-hour EC<sub>50</sub> was calculated to be 14 mg/L. Based on total biomass, the NOEC was determined to be 5.8 mg/L. The 0-72 hour E<sub>b</sub>C<sub>50</sub> was calculated to be 14 mg/L. Based on average growth rate, the NOEC was determined to be 12 mg/L. The 0-72 hour E<sub>r</sub>C<sub>50</sub> was calculated to be 16 mg/L. Cell densities in the 50 and 100 mg/L solutions that were adjusted to pH 7.5 were similar to that of the control, suggesting that the acidic nature of the non-pH adjusted MSA solution was probably the cause of algal inhibition.

## 2.4. Mammalian toxicity

### 2.4.1. Acute toxicity

Groups of five rats/sex were exposed by oral gavage to 300, 500 and 750 mg/kg bw anhydrous (99.6% pure) MSA (Elf Atochem, 1988). Clinical signs included salivation, decreased activity, wobbly gait, breathing abnormalities, apparent hypothermia, decreased/no defecation, feces small in size, urine stain, hunched posture, unkempt appearance, rough haircoat, piloerection, extremities pale in color, dehydration, emaciation, distended abdomen, decreased food consumption and dark material around the facial area. Body weight loss was noted for one male at 300 mg/kg bw, two females and one male at 500 mg/kg bw, and one male at 750 mg/kg bw during the study day 0-7. Body weight loss was noted for one male each at 300 mg/kg bw and 750 mg/kg bw during the study day 7-14. Body weight gain was noted for all other surviving animals during the test period. Gross pathology findings observed in the animals that died included distension/abnormal content/reddened mucosa in the digestive tract, dark red/mottled lungs, blackish-purple spleens, dark red lymph nodes, stained glandular mucosa in the stomach and body fat depletion/discoloration/adhesions in the abdominal cavity. Necropsy findings on study day 14 for the animals that survived included abnormal content in the digestive tract and thickened mucosa in the stomach. The acute oral LD<sub>50</sub> of anhydrous MSA in the male rat was greater than 750 mg/kg bw and 461 mg/kg bw in the female rat, and 649 mg/kg bw in the sexes combined.

Groups of five rats/sex were exposed by oral gavage to 500, 1000, and 1500 mg/kg bw 70% MSA in water (Elf Atochem, 1997a). Clinical signs included salivation, breathing abnormalities, wobbly gait, decreased activity, decreased defecation, rough haircoat, urine/fecal stain and dark material around the facial area. Body weight loss was noted for two animals at 1000 mg/kg bw during the study day 0-7 and for one animals each at 300 mg/kg bw 1000 mg/kg bw during the study day 7-14. Body weight gain was noted for all other surviving animals during the test period. Gross internal findings were observed only in the animals that died and included abnormal content and reddened/thickened mucosa and discoloration in the digestive tract, dark red foci on the liver and blackish-purple spleens. The acute oral LD<sub>50</sub> of 70% MSA in the male rat was 860 mg/kg bw, 2408 mg/kg bw in the female rat, and 1158 mg/kg bw in the sexes combined.

Five male rats were exposed by oral gavage to anhydrous MSA (98% pure) at 0.25, 0.5 ml/kg bw. Three rats were exposed at 1.0 ml/kg bw (Union Carbide, 1975). At all dose levels, rats were sluggish and presented an unsteady gait. In addition, at 1.0 ml/kg bw, deep breathing was immediately observed. At 0.25 ml/kg bw, 2/5 rats died. At 0.5 ml/kg bw 5/5 rats died; and at 1.0 ml/kg bw 2/3 rats died. Necropsy findings included livers mottled and burned, stomach burned, pylorus hemorrhaged and gas filled, intestines hemorrhaged, injected and gas filled, kidneys mottled and slightly congested. The LD<sub>50</sub> was 0.28 ml/kg bw.

In an OECD 402 test, one male New Zealand White rabbit was dosed dermally at 1000 mg/kg bw of 70% MSA in water (Atofina, 2002). Since no irritation was noted, an additional nine animals (4 males and 5 females) were dosed. The test article was kept in contact with the skin for 24 hours. Animals were observed for mortality, toxicity and pharmacological effects, body weights recorded and animals were examined for gross pathology. Dermal responses were recorded 24 hours post-dosing and on days 7 and 14. All animals survived the treatment. Instances of few feces were the only abnormal signs noted during the observation period. Dermal responses were slight to well-defined on day 1, absent to severe on day 7 and absent to slight on day 14. Body weight changes and necropsy results were normal. The LD<sub>50</sub> was greater than 1000 mg/kg bw.

Six albino rabbits were exposed to 200 and 2000 mg/kg bw anhydrous MSA (purity not specified) under occlusive cover for 24 hours (Pennwalt, 1978). Skin contact with 2000 mg/kg bw caused intense and prolonged pain. The skin was dark grey in appearance and scattered portions were

separating from the subcutaneous tissues. Two rabbits died and 1 rabbit was euthanized. There were no mortalities at 200 mg/kg bw. Erythema was present over the entire trunk of each animal together with numerous small lesions. There were no clinical signs and animals gained weight during the 7-day observation period. The LD<sub>50</sub> was greater than 200 and less than 2000 mg/kg bw.

#### **2.4.2. Genetic toxicity**

Bacterial reverse mutation assays (OECD 471) were conducted with anhydrous MSA (98.8% pure) (SNEAP, 1990) and 70% in water (Pennwalt, 1989a). No genotoxicity was observed on *Salmonella typhimurium* tester strains TA1535, TA1537, TA1538, TA98 and TA100 up to the cytotoxicity threshold of 5000 µg/plate in the presence and absence of metabolic activation.

Groups of five mice/sex were given a single dose of MSA (70% in water) by oral gavage at 20, 100 or 500 mg/kg bw (Pennwalt, 1989b). Concurrent vehicle and positive control group of mice were similarly dosed with distilled water or chlorambucil, respectively. The test method was comparable to OECD 474. There was no evidence of induced chromosomal or other damage leading to micronucleus formation in polychromatic erythrocytes of treated mice 24, 48 or 72 hours after oral administration.

#### **2.4.3. Repeated dose toxicity**

Five rats/sex were exposed by nose-only inhalation to MSA (69.9% aqueous solution) at concentrations of 0 (control) 0.026, 0.082, 0.23 and 0.74 mg/L for 6 hours/day for 5 days (Elf Atochem, 1996a). There were 2 and 3 deaths in the 0.23 and 0.74 mg/L groups, respectively. Rales were the only clinical sign observed in the 0.23 and 0.74 mg/L groups. Mean body weights and food consumption were generally reduced in males and females in the 0.74 mg/L group throughout the study. There were no effects on organ weights and no gross findings at necropsy. Microscopic findings in the nasal cavities included mucosal necrosis, suppurative inflammation and/or nasal exudate in males and females in the 0.23 and 0.74 mg/L groups. The NOEL for systemic toxicity was found to be 0.082 mg/L.

Fifteen rats/sex were exposed by nose-only inhalation to MSA (69.9% aqueous solution) at concentrations of 0 (control) 0.026, 0.073 and 0.242 mg/L for 6 hours/day for 5 days/week for four weeks (Elf Atochem, 1996b). There was a two-week recovery period following the 4-week exposure period. During the exposure phase of the study, 4, 1, 1 and 5 animals in the control, low-, mid- and high-exposure groups, respectively, were found dead. These deaths were not considered test article related. Clinical signs were reported only during the exposure period and consisted of rales and an increased incidence of yellow matting on various body surfaces in the high-exposure group animals. Matting was also observed in the mid-exposure group males. A transient reduction in mean body weight gain during the first week of exposure and slightly decreased food consumption throughout the exposure period were noted for the high-exposure group males. There were no effects on hematology, urinalysis, or organ weights. There was a statistically significant increase in blood urea nitrogen and aspartate aminotransferase in the high-exposure group males and females, respectively, at the study week 4 evaluations, but returned to levels comparable to the control group after the two-week recovery period. There were no test article related gross findings in the animals that were found dead during the study and no gross findings in animals at the end of the study. Test article-related microscopic findings were observed in the nasal turbinates of the high-exposure group rats that were found dead and in all treated groups at the study week 4 and 6 evaluations. The severity of some of the findings observed after the two-week recovery period suggested at least partial recovery from the irritative effects of the test article. Based on the compound-induced lesions observed in the nasal turbinates, the no observed effect level (NOEL) for

local irritation was considered to be less than 0.026 mg/L. The NOEL for systemic toxicity was considered to be 0.026 mg/L.

Five rats/sex were exposed to concentrations of MSA (98% anhydrous) in the diet of 0.043%, 0.159%, 0.382% and 1.635% (males) and 0.045%, 0.183%, 0.479% and 1.80% (females) for seven days (Union Carbide Corporation, 1975). These concentrations were equivalent to 0, 51, 185, 420, 1805 mg/kg bw/d (males) and 0, 55, 201, 551, 2122 mg/kg bw/d (females). There were no deaths, no effects on body weights or organ weights. The NOAEL was 1805 mg/kg/day for males and 2122 mg/kg/day for females.

#### **2.4.4. Reproductive toxicity**

In an OECD 421 study, groups of 12 rats/sex were exposed to MSA (70.5% in water) by oral gavage at doses of 250, 500 and 1000 mg/kg bw/d (Arkema and Chevron Phillips, 2005). Males were exposed 4 weeks before mating, during the mating period (2 weeks) and until sacrifice. Females were exposed 4 weeks before mating, during the mating period (2 weeks), pregnancy (3 weeks), lactation until day 4 postpartum (pp) inclusive, and until sacrifice (day 5 pp). One male animal died at 1000 mg/kg bw/day on day 33 and one female given 250 mg/kg bw/day was found dead on day 10 post-coitum. There were no test article related clinical signs of toxicity. There were no effects on body weights or food consumption. There were no effects on mating index, pre-coital interval, fertility index, duration of gestation, delivery data or postnatal and neonatal losses. There were no effects on the mean number of liveborn pups per litter. Minor differences, considered to be of no toxicological significance, were observed in the weights of testes and epididymides between treated and control males. Macroscopic post-mortem examination revealed no treatment-related effects. No microscopic treatment-related changes were observed for testicular staging or for the ovaries, including semi-quantitative evaluation of the morphological characteristics of ovarian physiology. The no observed effect level (NOEL) for parental toxicity and for toxic effect on reproductive performance and on progeny is 1000 mg/kg bw/day.

#### **2.4.5. Developmental toxicity**

A range finding study was conducted according to OECD 414 (Elf Atochem, 1996d). Groups of 8 female rats were exposed by oral gavage to doses of MSA (70.15% in water) of 0 (control), 25, 50, 100, 200 and 300 mg/kg bw/d on gestation days 5-15. Treatment-related clinical signs observed consisted of rales, labored respiration and gasping in the 100, 200 and 300 mg/kg bw/d groups. Findings of red material around the nose and/or mouth in the 100, 200 and 300 mg/kg/d groups often correlated with occurrences of the aforementioned respiratory abnormalities. These findings appeared to be a function of the dosage concentration; rather the dosage level, as they were observed with similar frequency in the 100, 200 and 300 mg/kg/d groups, each of which received the test article at a concentration of 50 mg/ml. There were no deaths. Slight mean body weight losses and reduction in food consumption occurred in the 100, 200 and 300 mg/kg bw/day groups during gestation days 6-9 when evaluated on a group mean basis. However, several animals in these groups experienced large, transient body weight losses and corresponding large decreases in food consumption on one or more occasions during the first days of the dosing period. Mean body weights, gravid uterine weights, net body weights and net body weight gains were unaffected by treatment at all dose levels. No treatment related internal necropsy findings were observed at any dose level. And no effects were observed at any dose level on intrauterine growth and survival. No external developmental variations of malformations were observed in any of the foetuses in the treated groups.

In an OECD 414 study, groups of 25 female rats were exposed to MSA (70.15% in water) by oral gavage at doses of 0 (control), 25, 100 and 400 mg/kg bw from gestation day 6 through 15 (Elf Atochem, 1996c). There were no test article related clinical signs and no deaths. There were no

effects on body weight or food consumption. At necropsy, intrauterine growth and survival were unaffected by test article administration at all dose levels. There were no test article related fetal malformations or developmental variations. A dose level of 400 mg/kg bw/day was considered to be the no observable adverse effect level (NOAEL) for maternal toxicity and developmental toxicity.

In an OECD 421 study, groups of 12 rats/sex were exposed to MSA (70.5% in water) by oral gavage at doses of 250, 500 and 1000 mg/kg bw/day (Arkema and Chevron Phillips, 2005). Males were exposed 4 weeks before mating, during the mating period (2 weeks) and until sacrifice. Females were exposed 4 weeks before mating, during the mating period (2 weeks), pregnancy (3 weeks), lactation until day 4 postpartum (pp) inclusive, and until sacrifice (day 5 pp). There were no effects on postnatal and neonatal losses; the mean number of liveborn pups per litter; pup mortality or clinical signs; pup body weight; or pup sex ratio. The NOEL for developmental effects was 1000 mg/kg bw/day.

### **3.0. Conclusion**

The available toxicity data for fish, aquatic invertebrates and aquatic plants indicates that methane sulfonic acid has a moderate potential to cause acute hazard to aquatic organisms. MSA is readily biodegradable and the low log  $K_{ow}$  value suggests that it has a low bioaccumulative potential. MSA is moderately toxic by oral and dermal exposure. It was not mutagenic and did not induce chromosomal changes. In a repeated dose toxicity study by inhalation exposure, a transient reduction in mean body weight gain and some microscopic findings in the nasal turbinates were the only adverse findings. The NOAEL for systemic toxicity was 0.026 mg/L. In a reproductive screening test, no effects for parental toxicity, reproductive performance and on progeny was observed up to the highest dosage tested (1000 mg/kg/day). No birth abnormalities were observed in the offsprings of rats given a dosage of 400 mg/kg/day during days 6 through 15 of pregnancy.

#### 4.0. References

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# I U C L I D

## Data Set

**Existing Chemical** : ID: 75-75-2  
**CAS No.** : 75-75-2  
**EINECS Name** : methanesulphonic acid  
**EC No.** : 200-898-6  
**Molecular Weight** : 96.1  
**Structural Formula** : CH3SO3H  
**Molecular Formula** : CH4O3S

**Producer related part**  
**Company** : ATOFINA Chemicals Inc.  
**Creation date** : 12.01.2006

**Substance related part**  
**Company** : ATOFINA Chemicals Inc.  
**Creation date** : 12.01.2006

**Status** :  
**Memo** :

**Printing date** : 10.10.2006  
**Revision date** :  
**Date of last update** : 17.03.2006

**Number of pages** : 85

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

# 1. General Information

Id 75-75-2  
Date 10.10.2006

## 1.0.1 APPLICANT AND COMPANY INFORMATION

Type : lead organisation  
Name : ARKEMA  
Contact person :  
Date :  
Street : 4-8, cours Michelet La Défense 10  
Town : 95091 Paris La Défense Cedex  
Country : France  
Phone :  
Telefax :  
Telex :  
Cedex :  
Email :  
Homepage :  
  
Source : Atofina Paris La Défense Cedex  
31.08.2005

## 1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

## 1.0.3 IDENTITY OF RECIPIENTS

## 1.0.4 DETAILS ON CATEGORY/TEMPLATE

### 1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name : Methanesulphonic acid  
Smiles Code :  
Molecular formula : C-H4-O3-S  
Molecular weight : 96.11  
Petrol class :  
  
Source : Atofina, Paris-la-Défense, France  
Atofina Paris La Défense Cede  
27.02.2006

#### 1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type : typical for marketed substance  
Substance type : organic  
Physical status : liquid  
Purity : > 99 % w/w  
Colour : light yellow  
Odour : Characteristic  
  
Source : Atofina, Paris-la-Défense, France  
Atofina Paris La Défense Cedex  
Reliability : None of the rats orally exposed to methane sulfonic acid (up to 1800 mg/kg/day) or to its potassium salt (2000 mg/kg/day) died during this 7-day study.

# 1. General Information

**Id** 75-75-2  
**Date** 10.10.2006

27.12.2002

Furthermore, none of the measured parameters (food consumption, body weight change, liver and kidney weight) was affected by the exposure. Consequently, NOAEL can be valued at 1805 mg/kg/day for males and 2122 mg/kg/day for females.

## 1.1.2 SPECTRA

## 1.2 SYNONYMS AND TRADENAMES

**methanesulfonic acid, MSA, methanesulfonic acid.**

**Source** : Atofina, Paris-la-Défense, France  
Atofina Paris La Défense Cedex

27.12.2002

## 1.3 IMPURITIES

## 1.4 ADDITIVES

## 1.5 TOTAL QUANTITY

## 1.6.1 LABELLING

## 1.6.2 CLASSIFICATION

## 1.6.3 PACKAGING

## 1.7 USE PATTERN

**Type of use** : use  
**Category** :

**Remark** : Acid Catalysts  
Chemical Manufacturing and Extraction  
Health and Pharmaceutical  
Leather and Textile Processing  
Metalworking and Metal Process.

**Source** : Atofina Paris La Défense Cedex  
22.02.2006

## 1.7.1 DETAILED USE PATTERN

## 1.7.2 METHODS OF MANUFACTURE

## 1.8 REGULATORY MEASURES

### 1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

### 1.8.2 ACCEPTABLE RESIDUES LEVELS

### 1.8.3 WATER POLLUTION

### 1.8.4 MAJOR ACCIDENT HAZARDS

### 1.8.5 AIR POLLUTION

### 1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

### 1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

### 1.9.2 COMPONENTS

## 1.10 SOURCE OF EXPOSURE

## 1.11 ADDITIONAL REMARKS

**Memo** : Transport information

**Remark** : UN number: 2586  
RID/ADR: class:8  
Item (letter): 34°C

Prescriptions: labels: 8.  
H.I. Nr/U.N. Nr: 80/2586

IMDG: class: 8  
packaging group: III  
UN Nr (IMDG): 2586

prescriptions: labels:corrosive/8

IATA: class: 8  
packaging group:III  
UN Nr: 2586

## 1. General Information

**Id** 75-75-2  
**Date** 10.10.2006

prescriptions: labels: corrosive/8

Further regulatory information:

RTMD R/F: class: 8

item (letter): 34°C

labels: 8

H.I. Nr/U.N. Nr: 80/2586

**Source** : Atofina, Paris-la-Défense, France  
Atofina Paris La Défense Cedex  
27.12.2002

### 1.12 LAST LITERATURE SEARCH

**Type of search** : Internal and External

**Chapters covered** : 3, 4, 5

**Date of search** : 31.08.2005

**Source** : ARKEMA, Paris-la-Défense, France  
Atofina Paris La Défense Cedex  
31.08.2005

### 1.13 REVIEWS

## 2.1 MELTING POINT

|                       |   |  |         |
|-----------------------|---|--|---------|
| <b>Value</b>          | : | = 19 °C  |         |
| <b>Decomposition</b>  | : | yes, at 225 °C   |         |
| <b>Sublimation</b>    | : |  |         |
| <b>Method</b>         | : | other  |         |
| <b>Year</b>           | : |  |         |
| <b>GLP</b>            | : | no data  |         |
| <b>Test substance</b> | : | other TS   |         |
| <b>Remark</b>         | : | Beginning of decomposition from: 200°C<br>Thermal decomposition giving toxic products: oxides of sulphur.<br>The product is stable at ambient temperature. |         |
| <b>Source</b>         | : | ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex   |         |
| <b>Test substance</b> | : | methane sulfonic acid anhydrous  |         |
| <b>Reliability</b>    | : | (2) valid with restrictions  |         |
| <b>Flag</b>           | : | Material Safety Dataset, Critical study for SIDS endpoint  |         |
| 27.12.2002            |   |  | (1) (6) |

## 2.2 BOILING POINT

|                       |   |  |     |
|-----------------------|---|--|-----|
| <b>Value</b>          | : | 167 °C at 13 hPa   |     |
| <b>Decomposition</b>  | : | no   |     |
| <b>Method</b>         | : |  |     |
| <b>Year</b>           | : |  |     |
| <b>GLP</b>            | : | no data  |     |
| <b>Test substance</b> | : | other TS   |     |
| <b>Remark</b>         | : | Decomposition 225°C.   |     |
| <b>Result</b>         | : | 229°C at 130 hPa   |     |
| <b>Source</b>         | : | ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex |     |
| <b>Test substance</b> | : | Methane sulfonic acid anhydrous.                                     |     |
| <b>Reliability</b>    | : | (2) valid with restrictions<br>data from handbook                    |     |
| <b>Flag</b>           | : | Material Safety Dataset, Critical study for SIDS endpoint            |     |
| 27.12.2002            |   |  | (7) |
| <b>Value</b>          | : | = 305 °C at 1033 hPa   |     |
| <b>Decomposition</b>  | : |  |     |
| <b>Method</b>         | : | other: calculated  |     |
| <b>Year</b>           | : |  |     |
| <b>GLP</b>            | : | no data  |     |
| <b>Test substance</b> | : |  |     |
| <b>Source</b>         | : | ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex |     |
| <b>Test substance</b> | : | Methane sulfonic acid anhydrous.                                     |     |
| <b>Reliability</b>    | : | (2) valid with restrictions<br>accepted calculation method           |     |
| <b>Flag</b>           | : | Material Safety Dataset  |     |
| 31.08.2005            |   |  | (1) |

## 2. Physico-Chemical Data

Id 75-75-2  
Date 10.10.2006

### 2.3 DENSITY

Type : density  
Value : = 1481 kg/m<sup>3</sup> at 18 °C  
Method : other  
Year :  
GLP : no data  
Test substance :

Source : ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex

Test substance : Methane sulfonic acid anhydrous.

Flag : Material Safety Dataset

17.02.1995

(1) (6)

### 2.3.1 GRANULOMETRY

### 2.4 VAPOUR PRESSURE

Value : = .013 hPa at 20 °C  
Decomposition :  
Method : Measured using an isoteniscope  
Year :  
GLP : no data  
Test substance : other TS

Source : ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex

Test substance : Methane sulfonic acid anhydrous.

Reliability : (2) valid with restrictions

Flag : Material Safety Dataset, Critical study for SIDS endpoint

12.01.2006

(1) (6)

### 2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water  
Log *p*<sub>ow</sub> : = -4.98 at °C  
pH value :  
Method : other (calculated)  
Year :  
GLP :  
Test substance : other TS

Source : ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex

Test substance : methane sulfonic acid

Reliability : (2) valid with restrictions

Accepted calculation method

Flag : Material Safety Dataset, Critical study for SIDS endpoint

12.01.2006

(26)

### 2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water

## 2. Physico-Chemical Data

Id 75-75-2  
Date 10.10.2006

|                               |   |  |               |
|-------------------------------|---|--|---------------|
| <b>Value</b>                  | : | 100 vol% at 20 °C  |               |
| <b>pH value</b>               | : |  |               |
| <b>concentration</b>          | : | at °C  |               |
| <b>Temperature effects</b>    | : |  |               |
| <b>Examine different pol.</b> | : |  |               |
| <b>pKa</b>                    | : | -1.92 at 25 °C   |               |
| <b>Description</b>            | : | miscible   |               |
| <b>Stable</b>                 | : |  |               |
| <b>Source</b>                 | : | ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex |               |
| <b>Test substance</b>         | : | Methane sulfonic acid anhydrous                                      |               |
| <b>Reliability</b>            | : | (2) valid with restrictions  |               |
| <b>Flag</b>                   | : | Material Safety Dataset, Critical study for SIDS endpoint            |               |
| 27.12.2002                    |   |  | (6) (27) (39) |
| <b>Solubility in</b>          | : | other: benzene   |               |
| <b>Value</b>                  | : | 1.5 vol% at 25 °C  |               |
| <b>pH value</b>               | : |  |               |
| <b>concentration</b>          | : | at °C  |               |
| <b>Temperature effects</b>    | : |  |               |
| <b>Examine different pol.</b> | : |  |               |
| <b>pKa</b>                    | : | at 25 °C   |               |
| <b>Description</b>            | : |  |               |
| <b>Stable</b>                 | : |  |               |
| <b>Source</b>                 | : | Atofina Paris La Défense Cedex                                       |               |
| <b>Test substance</b>         | : | Methane sulfonic acid anhydrous.<br>Data from handbook               |               |
| 17.12.2002                    |   |  | (7)           |

### 2.6.2 SURFACE TENSION

### 2.7 FLASH POINT

|                       |   |   |     |
|-----------------------|---|---|-----|
| <b>Value</b>          | : | = 189 °C  |     |
| <b>Type</b>           | : | closed cup  |     |
| <b>Method</b>         | : | other   |     |
| <b>Year</b>           | : |   |     |
| <b>GLP</b>            | : | no data   |     |
| <b>Test substance</b> | : |   |     |
| <b>Source</b>         | : | ELF ATOCHEM Paris la defense 10<br>EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)<br>Atofina Paris La Défense Cedex |     |
| <b>Test substance</b> | : | Methane sulfonic acid anhydrous.  |     |
| <b>Reliability</b>    | : | (2) valid with restrictions   |     |
| <b>Flag</b>           | : | Material Safety Dataset   |     |
| 31.08.2005            |   |   | (1) |

### 2.8 AUTO FLAMMABILITY

|                       |   |                  |  |
|-----------------------|---|------------------|--|
| <b>Value</b>          | : | > 500 °C at 1013 |  |
| <b>Method</b>         | : | other            |  |
| <b>Year</b>           | : |                  |  |
| <b>GLP</b>            | : | no data          |  |
| <b>Test substance</b> | : |                  |  |

## 2. Physico-Chemical Data

Id 75-75-2  
Date 10.10.2006

**Source** : ELF ATOCHEM Paris la defense 10  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
Atofina Paris La Défense Cedex  
**Test substance** : Methane sulfonic acid anhydrous.  
**Reliability** : (2) valid with restrictions  
**Flag** : Material Safety Dataset  
31.08.2005 (1)

### 2.9 FLAMMABILITY

### 2.10 EXPLOSIVE PROPERTIES

### 2.11 OXIDIZING PROPERTIES

### 2.12 DISSOCIATION CONSTANT

**Acid-base constant** : -1.86  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** : other TS  
**Source** : Atofina Paris La Défense Cedex  
**Test substance** : Methane sulfonic acid anhydrous.  
**Reliability** : (2) valid with restrictions  
31.08.2005 (40)

### 2.13 VISCOSITY

**Value** : - 13.5 mPa s (dynamic) at 20 °C  
**Result** :  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** : other TS: Anhydrous methanesulfonic acid  
**Source** : ARKEMA, Paris-la-Défense, France (JFR)  
Atofina Paris La Défense Cedex  
**Flag** : Material Safety Dataset  
02.01.2006 (6)

### 2.14 ADDITIONAL REMARKS

## 3.1.1 PHOTODEGRADATION

Type : air  
 Light source :  
 Light spectrum : nm  
 Relative intensity : based on intensity of sunlight  
 Deg. product :  
 Method : other (calculated)  
 Year :  
 GLP :  
 Test substance :

Remark : AOP Program (v1.90) Results:  
 =====  
 SMILES : O=S(=O)(O)C  
 CHEM : Methanesulfonic acid  
 MOL FOR: C1 H4 O3 S1  
 MOL WT : 96.10  
 -----SUMMARY (AOP v1.90): HYDROXYL RADICALS-----  
 \*\*Hydrogen Abstraction = 0.1360 E-12 cm3/molecule-sec  
 Reaction with N, S and -OH = 0.1400 E-12 cm3/molecule-sec  
 Addition to Triple Bonds = 0.0000 E-12 cm3/molecule-sec  
 Addition to Olefinic Bonds = 0.0000 E-12 cm3/molecule-sec  
 Addition to Aromatic Rings = 0.0000 E-12 cm3/molecule-sec  
 Addition to Fused Rings = 0.0000 E-12 cm3/molecule-sec  
  
 OVERALL OH Rate Constant = 0.2760 E-12 cm3/molecule-sec  
 HALF-LIFE = 38.754 Days (12-hr day; 1.5E6 OH/cm3)  
 .... \*\* Designates Estimation(s) Using ASSUMED Value(s)  
 ---SUMMARY (AOP v1.90): OZONE REACTION-----  
  
 \*\*\*\*\* NO OZONE REACTION ESTIMATION \*\*\*\*\*  
 (ONLY Olefins and Acetylenes are Estimated)  
  
 Experimental Database: NO Structure Matches  
 Source : Atofina Paris La Défense Cedex  
 Reliability : (2) valid with restrictions  
 Accepted calculation method  
 Flag : Critical study for SIDS endpoint  
 03.01.2003

## 3.1.2 STABILITY IN WATER

Type : abiotic  
 t1/2 pH4 : at °C  
 t1/2 pH7 : at °C  
 t1/2 pH9 : at °C

27.02.2006

## 3.1.3 STABILITY IN SOIL

## 3.2.1 MONITORING DATA

### 3. Environmental Fate and Pathways

Id 75-75-2  
Date 10.10.2006

#### 3.2.2 FIELD STUDIES

#### 3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III  
Media :  
Air : % (Fugacity Model Level I)  
Water : % (Fugacity Model Level I)  
Soil : % (Fugacity Model Level I)  
Biota : % (Fugacity Model Level II/III)  
Soil : % (Fugacity Model Level II/III)  
Method :  
Year :

Remark : Level III Fugacity Model (Full-Output):

=====  
Chem Name : Methanesulfonic acid  
Molecular Wt: 96.1  
Henry's LC : 1.26e-008 atm-m<sup>3</sup>/mole (Henrywin program)  
Vapor Press : 0.0267 mm Hg (Mpbpwin program)  
Liquid VP : 0.0272 mm Hg (super-cooled)  
Melting Pt : 25.8 deg C (Mpbpwin program)  
Log Kow : -2.38 (Kowwin program)  
Soil Koc : 0.00171 (calc by model)

|          | Mass Amount<br>(percent) | Half-Life<br>(hr) | Emissions<br>(kg/hr) |
|----------|--------------------------|-------------------|----------------------|
| Air      | 0.394                    | 930               | 1000                 |
| Water    | 45.6                     | 360               | 1000                 |
| Soil     | 54                       | 360               | 1000                 |
| Sediment | 0.0759                   | 1.44e+003         | 0                    |

|          | Fugacity<br>(atm) | Reaction<br>(kg/hr) | Advection<br>(kg/hr) | Reaction<br>(percent) | Advection<br>(percent) |
|----------|-------------------|---------------------|----------------------|-----------------------|------------------------|
| Air      | 1.25e-011         | 3.65                | 49                   | 0.122                 | 1.63                   |
| Water    | 3.71e-013         | 1.09e+003           | 566                  | 36.3                  | 18.9                   |
| Soil     | 1.63e-011         | 1.29e+003           | 0                    | 43                    | 0                      |
| Sediment | 3.09e-013         | 0.454               | 0.0189               | 0.0151                | 0.000629               |

Persistence Time: 414 hr  
Reaction Time: 521 hr  
Advection Time: 2.02e+003 hr  
Percent Reacted: 79.5  
Percent Adverted: 20.5

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):

Air: 930  
Water: 360  
Soil: 360  
Sediment: 1440  
Biowin estimate: 3.179 (weeks)

Advection Times (hr):

Air: 100  
Water: 1000  
Sediment: 5e+004

Source : Atofina Paris La Défense Cedex  
Reliability : (2) valid with restrictions  
Accepted calculation method

**Flag** : Critical study for SIDS endpoint  
03.01.2003

#### 3.3.2 DISTRIBUTION

#### 3.4 MODE OF DEGRADATION IN ACTUAL USE

#### 3.5 BIODEGRADATION

**Type** : aerobic  
**Inoculum** : domestic sewage  
**Concentration** : 11.3 mg/l related to COD (Chemical Oxygen Demand)  
related to  
**Contact time** : 28 day(s)  
**Degradation** : ca. 100 (±) % after 28 day(s)  
**Result** : readily biodegradable  
**Kinetic of testsubst.** : 3 day(s) = 4 %  
10 day(s) = 2 %  
17 day(s) = 15 %  
21 day(s) = 100 %  
28 day(s) = 100 %  
**Control substance** : Benzoic acid, sodium salt  
**Kinetic** : 3 day(s) = 97 %  
24 day(s) = 100 %  
**Deg. product** : not measured  
**Method** : OECD Guide-line 301 A (new version) "Ready Biodegradability: DOC Die  
Away Test"  
**Year** : 1992  
**GLP** : yes  
**Test substance** : other TS

**Result** : LATENT PERIOD: 10 days

VALIDITY CRITERIA:  
- Extreme values difference: <20%  
- Degradation of reference substance in 14 days: >60%  
- Inhibition: No (Degradation in inhibition flask in 14 days: >25%)

**Source** : Atofina, Paris-la-Défense, France  
Atofina Paris La Défense Cedex

**Test condition** : INOCULUM/TEST ORGANISM:  
- Type of sludge: Secondary effluent from a biologic treatment plant.  
- Sampling site: Versailles.  
- Preparation of inoculum: The effluent was taken the day before the sowing of flasks and was centrifuged at 20°C during 20 min at 4000g. The residue was diluted with test medium so that the concentration factor in comparison with the taken sample is about 140.  
- Initial cell concentration: 1.1 10E4 bacteria/ml.

TEST SYSTEM:  
- Culturing apparatus: 500 ml Erlenmeyer flasks, corked with carded cotton and gauze. Those flasks have been previously sterilised in an oven at 170°C for 1 hour.  
- Number of culture flasks per concentration: 2.  
- Aeration device: no data.

### 3. Environmental Fate and Pathways

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- Measuring equipment: Jenway 3410 (oxymeter, conductimeter, pH-meter), Maihak Tocor 100 (DOC analyzer).
- Closed vessels used: Yes.

INITIAL TEST SUBSTANCE CONCENTRATION: 11.3 mg DOC / L.

#### METHOD OF PREPARATION OF TEST SOLUTION:

A parent solution of methane sulfonic acid (titrated at 94 mg DOC/L) was diluted on the basis of 30 ml in 250 ml medium

DURATION OF THE TEST: 28 days.

ANALYTICAL PARAMETER: Dissolved Organic Carbon (DOC) is measured at each sampling time.

DOC degradation percentage is then calculated according the following formula:

$$Dt = [1 - (Ct/Cb0)/(C0-Cb0)] \times 100$$

with Ct: mean DOC concentration in culture medium containing test substance at t time

C0: initial mean DOC concentration in culture medium containing test substance

Cbt: mean DOC concentration in the blank culture medium at t time

Cb0: initial mean DOC concentration in the blank culture medium

SAMPLING: 0, 3, 7, 10, 14, 17, 21, 24 and 28 days.

#### TEST CONDITIONS

- Composition of medium:

.10 ml of solution a:  
8.5g KH<sub>2</sub>PO<sub>4</sub>  
21.75g K<sub>2</sub>HPO<sub>4</sub>  
33.4 g Na<sub>2</sub>HPO<sub>4</sub>·H<sub>2</sub>O  
0.5g NH<sub>4</sub>Cl  
q.s.p 1000ml ultrapure water.

.1 ml of solution b:  
27.5g CaCl<sub>2</sub> or 36.40g CaCl<sub>2</sub>·2H<sub>2</sub>O  
in 1000 ml of ultrapure water.

.1 ml of solution c:  
22.5g MgSO<sub>4</sub>·7H<sub>2</sub>O  
in 1000 ml of ultrapure water.

.1 ml of solution d:  
0.25g FeCl<sub>3</sub>·6H<sub>2</sub>O  
in 1000 ml of ultrapure water (this solution was prepared at the beginning of the test).

.ultrapure water q.s.p 1000 ml.

- pH: 7.4
- Additional substrate: No.
- Test temperature: 22+/-2°C.

INTERMEDIATES / DEGRADATION PRODUCTS: Not identified.

NITRATE/NITRITE MEASUREMENT: No.

**Test substance** : Test substance: methanesulfonic acid  
CAS no.: 75-75-2

### 3. Environmental Fate and Pathways

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Date 10.10.2006

|                                  |  |
|----------------------------------|--|
| <b>Conclusion</b>                | : Source: Elf Atochem<br>Batch number: 2690<br>Purity: 70% in water<br>: Aerobic biodegradation study of methane sulfonic acid shows a maximum biodegradation rate in 28 days (100%). This rate is reached as early as 21 days.<br><br>No physico-chemical degradation was observed (no abiotic degradation).<br><br>According to the OECD 301 guideline, methane sulfonic acid can therefore be considered as readily biodegradable.  |
| <b>Reliability Flag</b>          | : (1) valid without restriction<br>: Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint   |
| 12.01.2006                       | (22)   |
| <b>Type</b>                      | : aerobic  |
| <b>Inoculum</b>                  | : activated sludge, domestic   |
| <b>Contact time</b>              | : 68 day(s)  |
| <b>Degradation Result</b>        | : < 86.6 (±12) % after 55 day(s)   |
| <b>Kinetic of testsubst.</b>     | : 30 day(s) < 0 %<br>36 day(s) < 15 %<br>40 day(s) < 10 %<br>50 day(s) < 10 %<br>53 day(s) ca. 42 %  |
| <b>Control substance Kinetic</b> | : other: no data<br>: %<br>: %   |
| <b>Deg. product</b>              | : no   |
| <b>Method</b>                    | : OECD Guide-line 303 A "Simulation Test - Aerobic Sewage Treatment: Coupled Unit Test"  |
| <b>Year</b>                      | : 1981   |
| <b>GLP</b>                       | : no data  |
| <b>Test substance</b>            | : other TS   |
| <b>Result</b>                    | : See second and third attached document.<br><br>Methane sulfonic acid was introduced on day 13. Approximately 40 days were actually required to reach a steady biodegradation. The first 20 days showed a slight inhibition.  |
| <b>Source</b>                    | : Atofina, Paris-la-Défense, France<br>Atofina Paris La Défense Cedex  |
| <b>Test condition</b>            | : INOCULUM/TEST ORGANISM:<br>- Type of sludge: activated sludge from treatment plant<br>- Sampling site: Versailles<br>- Preparation of inoculum: a sixth of the reactor volume is renewed every day<br>- Initial cell concentration: no data<br><br>TEST SYSTEM:<br>- Culturing apparatus: waste water treatment model (see the first attached document)<br>- Number of culture flasks per concentration: one<br>- Aeration device: yes (see the first attached document)<br>- Measuring equipment: Dohrmann DC 80 analyzer<br>- Closed vessels used: no<br><br>INITIAL TEST SUBSTANCE CONCENTRATION: 20 mg/l |

### 3. Environmental Fate and Pathways

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#### METHOD OF PREPARATION OF TEST SOLUTION:

16 g of methane sulfonic acid (MSA) is dissolved in 1 litre ultrapure water. This solution is then diluted to the tenth in order to reach a 20 mg of organic carbon per litre.

DURATION OF THE TEST: 46 days

ANALYTICAL PARAMETER: COD, %COD (= (COD2-COD1)/COD2 x 100),

DR (= [ T - (E - E0)]/T x 100

COD2: COD measured at the exit of the model on D-day

COD1: COD measured at the entrance of the model on day D -1

DR: degradation

T: methane sulfonic acid concentration in synthetic waste water (in mg/l)

E: COD at the exit of the test model

E0: COD at the exit of the control model

SAMPLING: From day 0 to day 68

#### TEST CONDITIONS

- Composition of medium:

Nutritive solution:

. pancreatic pepton (Prolabo): 16 g

. beef meat extract (Biomérieux): 11 g

. urea (Labosi): 3 g

. NaCl: 0.7 g

. CaCl<sub>2</sub>, 2 H<sub>2</sub>O: 0.4 g

. MgSO<sub>4</sub>, 2 H<sub>2</sub>O: 0.2 g

. ultrapure water: qsp 1 L

Potassium phosphate solution :

. K<sub>2</sub>HPO<sub>4</sub>: 2.8 g

. Ultrapure water: qsp 1L

Eventual medium is composed of 10 ml of these two previous solutions, completed with 2 liters of urban water.

- pH: 6.07 to 8.41

- Additional substrate: no data

- Test temperature: 4°C

INTERMEDIATES / DEGRADATION PRODUCTS: Not identified.

NITRATE/NITRITE MEASUREMENT: yes

REFERENCE SUBSTANCE: no data

**Test substance** : Test substance: methanesulfonic acid

CAS no.: 75-75-2

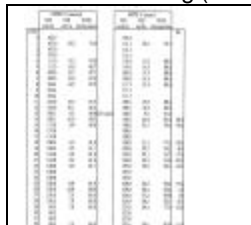
Source: Atochem

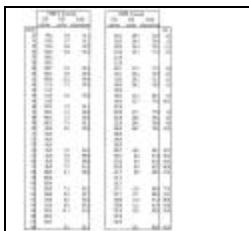
Batch number: 89 8015

Purity: no data

**Attached document** : 75-75-2 Biodeg (23567) Résultats 1.bmp

75-75-2 Biodeg (23567) Résultats 2.bmp





- Conclusion** : Mean biodegradation percentage from day 55 to day 68 was 86.6% (sd: 12.0%).  
This degradation was obtained at 20 mg of carbon per litre, that is to say 160 mg/l methane sulfonic acid.
- Methane sulfonic acid presents a good biodegradation potential in a waste water treatment plant, but only if it arrives steadily at the plant. Actually, sludge adaptation time was found to be very long here. This means punctual rejects would probably not be treated.
- Reliability** : (2) valid with restrictions  
**Flag** : Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint
- 31.08.2005 (41)
- Type** : aerobic  
**Inoculum** :  
**Deg. product** : yes  
**Method** : other: EPA, Methods for chemical analysis and wastes  
**Year** : 1979  
**GLP** : no data  
**Test substance** : other TS
- Remark** : Study peer reviewed  
**Result** : COD is not very representative of the potential oxygen demand for MSA. This could possibly due to the oxidation state of the compound or perhaps MSA is not completely oxidized by the potassium dichromate.
- Source** : Biodegradation inhibition was observed at 100 ppm.  
Atofina, Paris-la-Défense, France  
Atofina Paris La Défense Cedex
- Test condition** : INOCULUM/TEST ORGANISM:  
- Type of sludge: no data  
- Sampling site: Wyandott plant  
- Preparation of inoculum: no data  
- Initial cell concentration: no data
- TEST SYSTEM:  
- Culturing apparatus: no data.  
- Number of culture flasks per concentration: no data  
- Aeration device: no data  
- Measuring equipment: Ionics TOC analyzer  
- Closed vessels used: no data
- INITIAL TEST SUBSTANCE CONCENTRATION: 1, 10, 50 and 100 ppm
- METHOD OF PREPARATION OF TEST SOLUTION:  
Methane sulfonic acid (MSA) solutions were prepared by dilution of anhydrous MSA in lab distilled water.
- DURATION OF THE TEST: 4 weeks.

### 3. Environmental Fate and Pathways

Id 75-75-2  
Date 10.10.2006

|                          |  |
|--------------------------|--|
|                          | ANALYTICAL PARAMETER: COD, BOD and TOC   |
|                          | SAMPLING: Day 0, day 7, day 14 and day 21  |
|                          | TEST CONDITIONS  |
|                          | - Composition of medium: no data   |
|                          | - pH: no data  |
|                          | - Additional substrate: no data  |
|                          | - Test temperature: no data  |
|                          | INTERMEDIATES / DEGRADATION PRODUCTS: Not identified.  |
|                          | NITRATE/NITRITE MEASUREMENT: no data.  |
| <b>Test substance</b>    | REFERENCE SUBSTANCE: no data<br>: Test substance: methanesulfonic acid<br>C AS no.: 75-75-2<br>Source: no data<br>Batch number: PF 2690  |
| <b>Reliability</b>       | Purity: no data<br>: (4) not assignable<br>The lack of information does not allow a good appraisal of biodegradation. Readers should interpret the results with circumspection since test condition are not detailed enough.<br>This study is mentioned for the record only.   |
| 31.08.2005               | (3)  |
| <b>Type</b>              | : aerobic  |
| <b>Inoculum</b>          | : activated sludge, industrial   |
| <b>Contact time</b>      | : 20 day(s)  |
| <b>Degradation</b>       | : (±) % after  |
| <b>Result</b>            | : readily biodegradable  |
| <b>Control substance</b> | : other: none  |
| <b>Kinetic</b>           | : %<br>%   |
| <b>Deg. product</b>      | : not measured   |
| <b>Method</b>            | : other: NEN 3235-5.4 and 3235-5.3   |
| <b>Year</b>              | :  |
| <b>GLP</b>               | : no data  |
| <b>Test substance</b>    | : other TS   |
| <b>Remark</b>            | : Study peer reviewed  |
| <b>Result</b>            | : Discrepancies have been noted between text and table results. Since results presented in the table are more detailed, they are presented in attached document. However, they should be considered with caution.  |
|                          | Nevertheless, all results agree with no toxicity of methane sulfonic acid towards inoculum.  |
|                          | Methane sulfonic acid is nitrogen-free, nitrification did not occur. It has been checked.  |
| <b>Source</b>            | : Atofina, Paris-la-Défense, France<br>Atofina Paris La Défense Cedex  |
| <b>Test condition</b>    | : INOCULUM/TEST ORGANISM:<br>- Type of sludge: active sludge from an oxidation ditch. The oxidation ditch is used to treat domestic sewage.<br>- Sampling site: on the premises of TNO (Delft, Netherlands).<br>- Preparation of inoculum: The original sludge (2 g of solid substance /litre) was allowed to settle for 5 minutes and 2 ml of the supernatant was used to inoculate on litre of BOD |

### 3. Environmental Fate and Pathways

Id 75-75-2  
Date 10.10.2006

dilution water.  
- Initial cell concentration: no data

#### TEST SYSTEM:

- Culturing apparatus: BOD bottles
- Number of culture flasks per concentration: 4
- Aeration device: no data.
- Measuring equipment: oxygen electrode (OXI 191)
- Closed vessels used: no data

INITIAL TEST SUBSTANCE CONCENTRATION: 4, 8 and 16 mg/l.

#### METHOD OF PREPARATION OF TEST SOLUTION:

A stock solution containing 1600 mg methane sulfonic acid per litre BOD dilution water was prepared.

DURATION OF THE TEST: 20 days.

ANALYTICAL PARAMETER: Dissolved O<sub>2</sub> in the medium is measured after 5 and 20 days of exposure.

SAMPLING: 0, 5 and 20 days.

#### TEST CONDITIONS

- Composition of medium: no data
- pH: 7.13
- Additional substrate:
  - . solution containing glucose (3 g/l) and glutamic acid (3 g/l) up to 1 ml/l of the 16 mg/l MSA solution
  - . allylthiourea (1 mg/l added to a 8 mg/l MSA solution in order to detect nitrification influence)
- Test temperature: 20C.

INTERMEDIATES / DEGRADATION PRODUCTS: Not identified.

NITRATE/NITRITE MEASUREMENT: yes

REFERENCE SUBSTANCE: none

**Test substance** : Test substance: methanesulfonic acid  
CAS no.: 75-75-2  
Source: no data  
Batch number: no data  
Purity: 70% solution

**Attached document** : 75-75-2 BOD (TNO).bmp

| Time (h) | O <sub>2</sub> (mg/l) | BOD (mg O <sub>2</sub> /mg) |
|----------|-----------------------|-----------------------------|
| 0        | 0.00                  | 0.00                        |
| 5        | 0.05                  | 0.05                        |
| 10       | 0.10                  | 0.10                        |
| 15       | 0.15                  | 0.15                        |
| 20       | 0.20                  | 0.20                        |
| 25       | 0.25                  | 0.25                        |
| 30       | 0.30                  | 0.30                        |
| 35       | 0.35                  | 0.35                        |
| 40       | 0.40                  | 0.40                        |
| 45       | 0.45                  | 0.45                        |
| 50       | 0.50                  | 0.50                        |
| 55       | 0.51                  | 0.51                        |
| 60       | 0.51                  | 0.51                        |

**Conclusion** : No significant BOD<sub>5</sub> (20°C) was found.  
BOD<sub>20</sub> (20°C) was found to be 0.51 ± 0.04 mg O<sub>2</sub> per mg of methane sulfonic acid.  
Methane sulfonic acid could therefore be characterized as readily biodegradable.

**Reliability** : (3) invalid  
Discrepancies have been noticed between text and table results.

31.08.2005

(4)

### 3. Environmental Fate and Pathways

Id 75-75-2

Date 10.10.2006

|                       |   |  |
|-----------------------|---|--|
| <b>Type</b>           | : |  |
| <b>Inoculum</b>       | : | activated sludge   |
| <b>Deg. product</b>   | : |  |
| <b>Method</b>         | : | other:OECD 301 Modified OECD screening test (1993)   |
| <b>Year</b>           | : | 1993   |
| <b>GLP</b>            | : |  |
| <b>Test substance</b> | : |  |
| <b>Method</b>         | : | <p>A glass continuous culture (CC) bioreactor was used (see attached document figure 1). The volume of the bioreactor was 2.95 liters.</p> <p>Sludge loading was kept stable at approximately 6 g/l by appropriate wasting of mixed liquor suspended solids (MLSS). All chemicals used were reagent or HPLC grade materials and distilled water was used for all solution preparation.</p> <p>The vitamin and inorganic micronutrients solution was prepared as described in OECD guidelines. Except that all sulfate salts in the multiminerals solution were replaced with the corresponding chloride salts to help close the sulfur balance.</p>  |
| <b>Remark</b>         | : | <p>Frost (1991) identified that Escherichia coli K-12 bacteria can grow on MSA resulting in the complete mineralization of MSA to carbon dioxide and sulfate.</p> <p>The literature further suggests that the ability to utilize sulfonates as a source of carbon and energy is applicable to many other microorganisms.</p> <p>Methanesulfonate is used by diverse aerobic bacteria as a source of sulfur for growth, but is not known to be used by anaerobes either as sulfur source, a fermentation substrate, an electron acceptor.</p> <p>MSA has been identified as a major photochemical oxidation product of DMS. DMS and MSA are predominantly biogenic in origin and are the main gaseous links in the biogeochemical sulfur cycle.</p>   |
| <b>Source</b>         | : | <p>ATOFINA, PARIS -LA-DEFENSE, FRANCE.<br/>Atofina Paris La Défense Cedex</p>  |
| <b>Test condition</b> | : | <p>- Glass continuous culture (CC) Bioreactor:<br/>The MSA bioreactor influent nutrient solution (per litre) was prepared by adding:<br/>160 mg bacto beef extract, 110 mg bacto peptone, 90 mg bacto Urea, 0.6 ml ethanol and 0.6 ml methanol to the above OECD vitamin and inorganic micronutrient solution.<br/>The MSA bioreactor feed solution's BOD/N/P ratio was 100/5.7/1.1.<br/>- Pretreatment: no data</p> <p><b>STOCK AND TEST SOLUTION AND THEIR PREPARATION</b><br/>The MSA standard solution was prepared by weighing 1000 mg of MSA into 1 liter volumetric flask and diluting to the mark with distilled water.</p> <p>MSA concentrations were increased by a factor of -2 from 5 to 2000 mg/L during the course of this study. In addition, the amount of sodium bicarbonate added to the MSA bioreactor solution for buffering was increased from 0.75 to 1.5 g/L with increasing MSA concentrations.</p> <p><b>DILUTION WATER</b><br/>- Source: Distilled water was used for all solution</p> |

preparations.

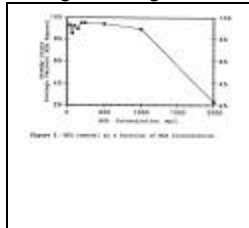
pH: The pH was monitored throughout the study and was maintained in the range 6.8 to 7.8 through the addition of Sodium bicarbonate.

TEST SYSTEM

- Exposure schedule: The hydraulic residence time (HRT) was maintained at approximately 60 hours. The optimum HRT for the microorganisms in the bioreactor was found to be  $\geq 40$  and  $\leq 60$  hours.

MONITORING OF TEST SUBSTANCE CONCENTRATION: IC analysis of MSA, chloride, phosphate, sulfate and nitrate was conducted using a Dionex DX300 ion chromatography system. The anions are separated using the HPIC-AS4A exchange separator column.

Attached document : Magliette figure 2.bmp



Conclusion : The activated sludge organisms were gradually challenged with increasing MSA concentrations ( a factor of  $\leq 2$ ). Rapid increase in MSA concentrations were found to be inhibitory. Higher MSA concentrations (2000 mg/L) were found to be inhibitory to the activated sludge organisms.

As long as the MSA concentration does not exceed 1000 mg/L, the sewerage of MSA to a well acclimated activated sludge treatment plant should pose no acute adverse impact on its performance.

These results suggest that MSA degradants are ubiquitous and abundant in nature.

Baker et al (1991) postulated that the sulfonic acid functional group of MSA must be available for microbial utilization. They also demonstrated that the methylotrophs and sulfur bacteria are able to derive energy from the degradation of MSA.

Results of this study indicate that microorganisms naturally present in any activated sludge wastewater treatment plant can be acclimated to degrade MSA.

Microorganisms play a vital role in the biogeochemical sulfur cycle.

Reliability : (4) not assignable  
02.01.2006

(28)

Type : aerobic  
Inoculum :

Remark : Methanesulfonate offers a number of hypothetical possibilities for use as a substrate for microbial growth and metabolism. It could provide sulfur for biosynthesis to any organism able to cleave the C-S bond under aerobic or anaerobic conditions.

It could undergo oxidation to carbon dioxide and sulfate, yielding metabolic energy for growth from the oxidation of methyl -groups, and even of the sulfonate moiety to sulfate. Its methyl group could provide carbon intermediates for Methylophilic bacteria.

It might be used anaerobically either as a terminal electron acceptor for anaerobic respiration, as a substrate for fermentative disproportionation or even as a substrate for methanogenesis from its methyl groups by archaeal methanogens.

Methanesulfonic acid is a very stable strong acid and a key intermediate in the biogeochemical cycling of sulfur.

Methane sulfonate oxidation is initiated by cleavage catalysed by methanesulfonate monooxygenase. Apart from very limited mention of methanesulfonic acid as a sulphur source for some organisms, no work had at that time been done to investigate the microbial degradation of this important intermediate in the global sulphur cycle.

Methanesulfonate is remarkably stable. Such data indicate that the absence of detectable methanesulfonate from soils and the marine environment is because of its biological rather than chemical degradation.

Methanesulfonate has thus had a continuous and significant input to marine and terrestrial environments. Ample time was thus available for the evolution of bacteria able to use methanesulfonate, and the absence of measurable quantities from soils and water indicates its ready degradation by the modern microflora.

The methanesulfonate monooxygenase of *Methylosulfonomonas* and *Marinosulfonomonas*:

Cell-free extracts of strain M2 contained a cytoplasmic methanesulfonate monooxygenase activity that was specifically induced by growth on methanesulfonate and catalysed methanesulfonate-dependent NADH.

The methanesulfonate monooxygenase of strain M2 was resolved into three distinct fractions, none with individual methanesulfonate oxidizing activity, but which together were reconstituted into an active form.

It has been possible to design gene-specific primers to analyse newly isolated methanesulfonate users from a variety of different environments by using the sequences determined for the highly conserved *msmA* from *Methylosulfonomonas* strain M2 and *Marinosulfonomonas* strain TR3.

DNA was extracted directly from aerobic enrichment cultures, with methanesulfonic as the sole substrate, using inocula from soil, sediment and marine samples.

These observations strongly support the view that a conserved methanesulfonic monooxygenase enzyme is present in a variety of bacterial genera and consequently enables the use of molecular techniques for the direct study of environmental samples.

**Source** : ATOFINA, PARIS -LA-DEFENSE, FRANCE  
Atofina Paris La Défense Cedex

**Conclusion** : -Methanesulfonate as a sulfur source  
Numerous longer-chain sulfonates are used as sulfur sources for growth by diverse bacteria, fungi and algae. But the use

of methanesulfonate seems to be more restricted. Methanesulfonate is the most stable sulfonate and the poorest sulfur source. A number of aerobic bacteria can use methanesulfonate as a sulfur source.

-Methanesulfonate as a respiratory electron acceptor, fermentation substrate or methanogenic substrate.

To date no bacteria have been described that can degrade methanesulfonate in the absence of oxygen. But the possibility to find anaerobic methanesulfonate degraders cannot be excluded.

Methanesulfonate is an analogue of methanephosphonate, which had been shown to be degraded by *Comamonas testosteroni* to produce methane and phosphate by hydrolytic cleavage of the C-P bond.

Methanesulfonate has not yet been shown to be a respiratory electron acceptor for any sulfate-reducing bacterium. Use of methanesulfonate or its hydrolysis products as respiratory hydrogen acceptors by the action of methanogens or sulfate reducers could conceivably lead to its anaerobic mineralization to methane and sulfite or sulfide.

-Methylotrophic growth on methanesulfonate as a source of carbon and energy.

Desulfonation of methanesulfonic can lead initially only to methanol or formaldehyde. Thus only methylotrophic bacteria are likely to be able to use methanesulfonate as the sole substrate for growth as any non-methylotrophic heterotroph possessing a methanesulfonate monooxygenase enzyme would not be able to derive cell-carbon exclusively from methanesulfonate, although the oxidation of methanesulfonate to carbon dioxide and water could act as a supplementary energy source.

The first bacterium isolated on methanesulfonate as sole substrate was characterized as belonging to a novel genus within the  $\alpha$ -proteobacteria, *Methylosulfonomonas* (soils).

These observations and the inability of some other well-known genera of methylotrophs to use methanesulfonate, suggested that methanesulfonate use might be restricted to these specialized genera.

-Mechanism of growth on methanesulfonate

All of the aerobic bacteria shown to date to use linear alkanesulfonate as growth substrates probably use a monooxygenase to split the C-S bond of the sulfonate. Hydrolysis of methanesulfonate to produce methanol does not occur in any of the methylotrophs isolated so far.

The observations strongly support the view that a conserved methanesulfonic monooxygenase enzyme is present in a variety of bacterial genera and consequently enables the use of molecular techniques for the direct study of environmental samples.

**Reliability**  
02.01.2006

: (4) not assignable

(31)

**Remark**

: This paper describes the initial purification and characterization of an MSA-monooxygenase (MSAMO), capable of C-S bond fission in the presence of NADH, from methylotroph

strain M2, and also the isolation of mutants of strain M2 lacking the ability to carry out such a reaction.

A major product of DMS oxidation reactions can be methanesulfonic acid (MSA), a stable strong acid that does not undergo photochemical oxidation.

Once deposited on the earth, MSA is thought to undergo biodegradation ultimately to form CO<sub>2</sub> and SO<sub>4</sub><sup>2-</sup>, which in turn can be incorporated into DMSP (dimethylsulfoniopropionate), thus completing part of the biogeochemical organic sulfur cycle.

The stability of MSA is due mainly to the strength of the C-S bond found in all organosulfate compounds.

Aliphatic sulfonates have been also identified as sole sulfur sources for bacteria isolated from soil and sewage, as well as certain enteric bacteria and some yeasts. Bacteria have also been isolated which can utilize both primary and secondary alkyl sulfonates as the only source of carbon and energy.

In both cases, primary biodegradation is proposed to be by direct desulfonation of the alkyl sulfonate. The mechanism proposed involves the insertion of a hydroxyl group at the α-carbon by a monooxygenase enzyme.

Initial studies on the utilization of MSA as a sole source of carbon and energy by the methylotroph M2; Kelly have indicated that the initial step involves desulfonation to produce formaldehyde and sulfite.

Initial studies with cell-free extracts of strain M2 have identified an enzyme capable of oxidising MSA in the presence of NADH.

The enzyme is cytosolic and is induced in strain M2 only when grown on MSA as sole carbon and energy source. The enzyme had:

- pH optimum of 7-7.2
- and was stable for several days at -20°C
- no appreciable loss of activity was observed after 5 weeks at -70°C.

#### Result

- : MSAMO activity and inhibition in cell-free extracts  
Initial studies with freshly prepared cell free extracts of MSA-grown strain M2 had revealed an enzyme capable of oxidising MSA in the presence of NADH.

Inhibition of the enzyme by metal chelators (bathophenanthroline, bathocuproine, neocuproine and sodium EDTA) indicated that the enzyme did indeed have associated metal ions, which are required for activity. Electron transfer reactions were essential to the reactions producing cleavage of the C-S bond of MSA.

Isolations of mutants, which could not utilize methanol as sole carbon and energy source, but which were still able to utilize MSA, supports the proposed MSA oxidation pathway in strain M2, whereby MSA is oxidised directly to formaldehyde and sulfite, but methanol is not an intermediate in the pathway.

The ability of methanol mutants to grow at the expense of MSA confirmed that methanol was not an obligatory intermediate of the MSA degradative pathway in strain M2.

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|                       |  |
|-----------------------|--|
|                       | <p>Elimination of methanol as a potential intermediate of MSA biodegradation and the production of sulfite by cell extracts of strain M2 is consistent with an oxygenolytic mechanism.</p> <p>The ability of MSAMO to desulfonate only short-chain sulfonates suggests the metabolism of primary aliphatic sulfonates by different enzymes may be carbon-chain-length dependent.</p> <p>The isolation of both structural and regulatory mutants of MSA metabolism facilitates their use in future-studies concerning the regulation of MSA oxidation pathways. These double mutants could also be transport mutants lacking the ability to take up both MSA and formate into the cell.</p>   |
| <b>Source</b>         | : ATOFINA, PARIS -LA-DEFENSE, FRANCE.<br>Atofina Paris La Défense Cedex  |
| <b>Test condition</b> | : Growth of the organisms and preparation of cell-free extracts:<br>Methylotriph strain M2 was cultivated and maintained on mineral salts medium. Trace element solution and vitamin solution were added only when carbon substrates were added to give a final concentration of 20 mM.<br>15 g/l of Difco bacto agar was added to the medium prior to sterilization.  |
|                       | <p>Initially a batch culture of strain M2 was grown in 5000 ml fermenter equipped with pH, oxygen and temperature control.</p> <ul style="list-style-type: none"><li>- Temperature: 30 °C</li><li>- pH: 7</li><li>- Air was supplied to the fermenter continuously at 1 ml (ml culture<sup>-1</sup>) min<sup>-1</sup></li></ul> <p>- Treatment: Cells were harvested by centrifugation (17000 g) at 4°C, washed three times with 40 mM Tris/HCl buffer. The cells were either drop-frozen in liquid nitrogen prior to storage at - 70°C or immediately broken by two or three passages through a chilled French pressure cell at 137 MPa. Cell debris was removed by centrifugation (50 000 g) for 75 min at 4°C to yield the cell-free extract which was immediately used, or drop -frozen in liquid nitrogen and stored at - 70°C.</p> <p>- Analytical methods: The protein content of cell extracts was determined by the methods of Bradford. Analysis of cell extracts and protein fractions was carried out on 1 2% (W/V) acrylamide gel.</p> <p>- Whole-cell oxygen electrode studies. Only 20-30 mg dry weights of washed cells were used in each experiment and the change in oxygen uptake was determined after the addition of 1 mM (final concentration) of each substrate.</p> <p>- Enzyme assay: A modification of the spectrophotometer assay for measuring MSA monooxygenase activity was used, based on monitoring the substance-simulated oxidation of NADH at 340 nm where 2 nmol FAD and 100 nmol Fe(NH<sub>4</sub>)<sub>2</sub>(SO<sub>4</sub>)<sub>2</sub> were also added to the reaction mixture. This assay was based on the detection of sulfite produced following MSA oxidation.</p> |

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Mutagenesis: Was terminated after incubation with shaking (200 r.p.m) at 30°C for sufficient time (23-25 min). Washed cells were resuspended in 200 ml sterile Min E medium and allowed to recover by incubation with shaking at 30°C for 24 hours in the presence of vitamin solution, trace element solution, 20 mM each of MSA, methylamine, formate, and 0,2 % (v/v) methanol. The cells were then subjected to penicillin-enrichissement by centrifugation and resuspension in Min E medium.

**Conclusion** : The initial step in the biodegradative pathway of MSA in strain M2 involved an inducible NADH-specific monooxygenase enzyme (MSAMO). Analysis of mutants of strain M2 defective in the metabolism of C, compounds indicated that methanol was not an intermediate in the degradative pathway of MSA and also confirmed the involvement of a multicomponent enzyme in the degradation of MSA by methylotroph strain M2.

**Reliability** : (4) not assignable  
30.12.2002 (30)

#### 3.6 BOD5, COD OR BOD5/COD RATIO

#### 3.7 BIOACCUMULATION

#### 3.8 ADDITIONAL REMARKS

## 4.1 ACUTE/PROLONGED TOXICITY TO FISH

|                              |   |   |
|------------------------------|---|---|
| <b>Type</b>                  | : | static  |
| <b>Species</b>               | : | Oncorhynchus mykiss (Fish, fresh water)   |
| <b>Exposure period</b>       | : | 96 hour(s)  |
| <b>Unit</b>                  | : | mg/l  |
| <b>NOEC</b>                  | : | = 56  |
| <b>LC50</b>                  | : | = 73  |
| <b>Limit test</b>            | : |   |
| <b>Analytical monitoring</b> | : | yes   |
| <b>Method</b>                | : | OECD Guide-line 203 "Fish, Acute Toxicity Test"   |
| <b>Year</b>                  | : | 1992  |
| <b>GLP</b>                   | : | yes   |
| <b>Test substance</b>        | : | other TS  |
| <b>Result</b>                | : | <p><b>RESULTS: RANGE FINDING TEST:</b><br/>Prior to initiating the definitive study, a preliminary test was conducted during which rainbow trout were exposed under static conditions to nominal concentrations of 0, 0.10, 1.0, 10, 40 and 100 mg/l MSA. Mortality of 100% was observed among rainbow trout exposed to the 100 mg A.I./L treatment level following 24 hours of exposure. At test termination (96 hours), no mortality or adverse effects were observed among the rainbow trout exposed to the 0.10 to 40 mg A.I. (active ingredient)/L. treatments or the control. Based on these results, nominal concentrations of 13, 22, 37, 60 and 100 mg A.I./L were selected for the definitive study.</p> <p>In an effort to evaluate the effect of pH on the toxicity of the test substance to the exposed organisms, a duplicate set of exposure solutions was established at the 60 and 100 mg A.I./L treatment levels. The pH of these solutions was adjusted to 7.1 - 7.3 with sodium hydroxide.</p> <p><b>RESULTS: EXPOSED</b></p> <ul style="list-style-type: none"> <li>- Nominal/measured concentrations: Measured concentrations were within 86% of nominal</li> <li>- Mortality and effect data: 100% mortality at 96 mg/l group only</li> <li>- Concentration / response curve:<br/>See Attached Document 5</li> </ul> |
| <b>Source</b>                | : | Atofina, Paris-la-Défense, France<br>Atofina Paris La Défense Cedex   |
| <b>Test condition</b>        | : | <p><b>TEST ORGANISMS</b></p> <ul style="list-style-type: none"> <li>- Supplier: Springborn culture facility</li> <li>- Wild caught: no</li> <li>- Post-hatch transfer time: no data</li> <li>- Age: no data</li> <li>- Size: 45 mm (range 40 to 54 mm)</li> <li>- Weight: 0.86 (range 0.57 to 1.43 g)</li> <li>- Feeding: food was stopped 24-h prior to test initiation</li> <li>- Pretreatment: Prior to testing, the fish were held in a 500-L fiberglass tank under a photoperiod of 16h light and 8h darkness for 14 days. No mortality was observed during the 48-h period prior to testing.</li> <li>- Feeding during test: No</li> <li>- Controls: Yes</li> </ul>   |

## STOCK AND TEST SOLUTION AND THEIR PREPARATION

- Dispersion: A 50 mg/ml stock solution was prepared by dissolving 35.36 g of methane sulfonic acid (from a 70% solution) in 500 ml of distilled water. Treatment level solutions were prepared by adding the appropriate amount of the 50 mg A.I. (Active Ingredient)/ml to the 15L of dilution water.
- Vehicle, solvent: water (the same as that used in the fish holding tank)

## DILUTION WATER

- Source: from a 100-meter deep bedrock well and well water supplied by the Town of Wareham, Massachusetts.
- Aeration: yes
- Alkalinity: 40 mg/l (CaCO<sub>3</sub>)
- Hardness: 34 mg/l (CaCO<sub>3</sub>)
- Salinity: 10 mg/l
- TOC (Total Organic Carbon): 0.57 mg/l
- TSS: 0.0 mg/l
- pH: 7.3
- Oxygen content: 76 to 86%
- Conductance: 100 to 145 µmhos/cm

## TEST SYSTEM

- Concentrations: 13, 22, 37, 60 and 100 mg A.I./L
- Renewal of test solution: no
- Exposure vessel type: 18.9 -L glass aquarium, containing 15L of test solution
- Number of replicates: 2
- Number of individuals per replicate: 10
- Test temperature: 12°C
- pH: cf. Attached document 1
- Adjustment of pH: In order to evaluate the effect of pH on the toxicity of the substance, a duplicate set of exposure solutions was established at the 60 and 100 mg A.I./L treatment level. The pH of these solutions was adjusted to 7.1 to 7.3 with a 4.0 NaOH solution.
- Intensity of irradiation: 80 footcandles at the solution's surface
- Photoperiod: 16h light / 8h darkness

## ENDPOINTS ASSESSED:

Fishes: mortality (dead fishes were removed twice a day), sublethal effects, LC50 and NOEC  
 Water: physical observations (precipitate, film on surface), pH, dissolved oxygen, temperature, total alkalinity, methane sulfonic acid concentration (titrated at 0 and 96 hours in all replicate solutions)

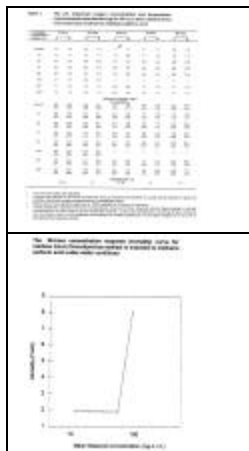
## MONITORING OF TEST SUBSTANCE CONCENTRATION:

Analytical device: HPLC

## STATISTICAL TEST:

Moving average angles, Probit analysis

- Test substance** : Source: Elf Atochem  
Batch number: 2324E20HD1  
Purity: 70.3%
- Attached document** : pH.bmp  
75-75-2 Acute tox. to fish (97-4-7192) Dose-response curve.bmp



- Conclusion** : The 96-hour LC50 was estimated by nonlinear interpolation to be 73 mg A.I./L with a 95% confidence interval, calculated by binomial probability to be 56 to 96 mg A.I./L. The NOEC was determined to be 56 mg A.I./L. No mortality was noted in the 62 and 89 mg A.I./L solutions which were adjusted to pH 7.1 to 7.3.
- Reliability Flag** : (1) valid without restriction  
: Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint

12.01.2006

(21)

#### 4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

- Type** : static  
**Species** : Daphnia magna (Crustacea)  
**Exposure period** : 48 hour(s)  
**Unit** : mg/l  
**NOEC** : = 120  
**EC50** : = 260  
**Analytical monitoring** : yes  
**Method** : OECD Guide-line 202  
**Year** : 1981  
**GLP** : yes  
**Test substance** :
- Method** : - Analytical device: General Electric type 217 light-meter, Spring Instrument Company (YSI) model 33 salinity-conductivity-temperature-meter, Hanna model HI9024 pH-meter, YSI dissolved oxygen-meter, Fisher Scientific Min-Max thermometer, HPLC.  
 - Statistical test: Moving average angle and probit analysis
- Remark Result** : Study peer reviewed  
 : Based on measured concentrations, the 48-hour EC50 value was estimated by nonlinear interpolation to be 260 mg A.I./L with 95% confidence limits calculated by binomial probability of 210 to 330 mg A.I./L.

The No-Observed-Effect Concentration (NOEC) through 48 hours was determined to be 120 mg A.I./L.

Immobilization in the 620 and 900 mg A.I./L solutions which were adjusted to pH 7.9 to 8.3 were similar to that of the control. These data indicate that the acidic nature of the non pH adjusted test solution probably contributed to the

|                       |   |
|-----------------------|---|
| <b>Source</b>         | : immobilization observed during the definitive test.<br>: Atofina, Paris-la-Défense, France<br>Atofina Paris La Défense Cedex  |
| <b>Test condition</b> | : TEST ORGANISMS<br>- Source/Supplier: Springborn Laboratories culture facility<br>- Breeding method: no specific data<br>- Age: < 24 hours<br>- Feeding: Ankistrodesmus falcatus (unicellular green algae)<br>2ml of a 4.10E7 cell/ml suspension per day in each vessel.<br>- Pretreatment: no data<br>- Feeding during test: no<br>- Control group: yes<br><br>STOCK AND TEST SOLUTION AND THEIR PREPARATION<br>- Dispersion: a 50 mg A.I./L stock solution was prepared by diluting 7.1124 g of the 70% solution of methane sulfonic acid with distilled water up to 100 ml.<br>- Vehicle, solvent: water<br>- Concentration of vehicle/solvent: no data<br><br>REFERENCE SUBSTANCE: no<br><br>DILUTION WATER<br>- Source: fortified well water and filtered through an Amberlite XAD-7 resin column<br>- Composition:<br>Total hardness as CaCO <sub>3</sub> : 170 mg A.I./L<br>Total alkalinity as CaCO <sub>3</sub> : 120 mg A.I./L<br><br>PRELIMINARY STUDY: yes, range-finding study<br><br>TEST SYSTEM<br>- Concentrations: 120, 210, 330, 570 and 890 mg A.I./L<br>- Renewal of test solution: no<br>- Exposure vessel type: 1-litre glass beaker, containing 500 ml of test solution<br>- Number of replicates: 2<br>- Number of individuals per replicate: 5<br>- Test temperature: 19 to 21°C<br>- Dissolved oxygen: 8.0 to 8.2 mg/l<br>- pH: 8.3<br>- Adjustment of pH: between 7.9 and 8.3, only for a duplicate set including 600 and 1000 mg A.I./L<br>- Intensity of irradiation: 60 footcandles at the solution surface<br>- Photoperiod: 16 hours of light + 8 hours darkness<br><br>DURATION OF THE TEST: 24 and 48 hours<br><br>QUALITY CRITERIA:<br>- Control mortality (OK if < 10%):<br>- pH (OK if equals to initial pH ± 1): not fulfilled in the 330 mg/l flask<br>- Dissolved oxygen (OK if > 2mg/L): OK<br>- Test substance concentration (OK if > 80% of initial concentration): OK<br><br>MONITORING OF TEST SUBSTANCE CONCENTRATION:<br>One water sample was removed from both replicate solutions of each treatment level and the controls at 0 and 48 hours for the analysis of methane sulfonic acid concentration. |
| <b>Test substance</b> | : Test substance: methanesulfonic acid  |

## 4. Ecotoxicity

Id 75-75-2

Date 10.10.2006

CAS no.: 75-75-2  
Source: Elf Atochem  
Batch number: 2324E20HD1  
Purity: 70.3% in water

**Reliability Flag** : (1) valid without restriction  
: Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint

31.08.2005 (20)

**Type** :  
**Species** : Daphnia magna (Crustacea)  
**Exposure period** : 24 hour(s)  
**Unit** : mg/l  
**EC50** : = 1.7  
**EC100** : = 7.405 calculated  
**Analytical monitoring Method** : no  
: ISO 6341 15 "Water quality - Determination of the inhibition of the mobility of Daphnia magna Straus (Cladocera, Crustacea)"

**Year** :  
**GLP** : no  
**Test substance** :

**Result** : NOEC: undetermined  
EC50: 1.7 mg/l  
EC100: 7.405 mg/l

**Source** : EC50 with potassium dichromate: 1.0 mg/l  
: ELF ATOCHEM Paris la defense 10  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
Atofina Paris La Défense Cedex

**Test condition** : TEST ORGANISMS  
- Source/Supplier: no data  
- Breeding method: synthetic medium  
- Age: no data  
- Feeding: (Scenedesmus subspicatus) + Tetramin  
- Pretreatment: no data  
- Feeding during test: algae  
- Control group: yes

STOCK AND TEST SOLUTION AND THEIR PREPARATION  
- Dispersion: no data  
- Vehicle, solvent: water  
- Concentration of vehicle/solvent: no data  
- Other procedures: no data

STABILITY OF THE TEST CHEMICAL SOLUTIONS: no data

REFERENCE SUBSTANCE: potassium dichromate

DILUTION WATER  
- Source: no data  
- Composition: no data

PRELIMINARY STUDY: no data

TEST SYSTEM  
- Concentrations: no data  
- Renewal of test solution: no data  
- Exposure vessel type: no data  
- Number of replicates: no data  
- Number of individuals per replicate: no data  
- Test temperature: no data

## 4. Ecotoxicity

Id 75-75-2  
Date 10.10.2006

|                        |   |
|------------------------|---|
|                        | - Dissolved oxygen: 9.0 mg/l<br>- pH: 3.51<br>- Adjustment of pH : no data<br>- Intensity of irradiation: no data<br>- Photoperiod: no data   |
|                        | QUALITY CRITERIA:<br>- Control mortality (OK if < 10%): no data<br>- pH (OK if equals to initial pH $\pm$ 1): no data<br>- Dissolved oxygen (OK if > 2mg/L): OK<br>- Test substance concentration (OK if > 80% of initial concentration): no data   |
|                        | SAMPLING: no data   |
|                        | MONITORING OF TEST SUBSTANCE CONCENTRATION: no data   |
| <b>Test substance</b>  | : Test substance: methanesulfonic acid<br>C AS no.: 75-75-2<br>Source: Atochem<br>Batch number: 1228/89<br>Purity: no data  |
| <b>Reliability</b>     | : (4) not assignable<br>Documentation insufficient for assessment.  |
| 02.01.2006             | (23)  |
| <b>Type</b>            | : static  |
| <b>Species</b>         | : Daphnia pulex (Crustacea)   |
| <b>Exposure period</b> | :   |
| <b>Unit</b>            | :   |
| <b>Remark</b>          | : Study peer reviewed   |
| <b>Result</b>          | : Average tolerance level, 24h = 33 mg/l<br>Average tolerance level, 48h = 12 mg/l  |
| <b>Source</b>          | : Atofina, Paris-la-Défense, France<br>Atofina Paris La Défense Cedex   |
| <b>Test condition</b>  | : Werner's method was applied (WERNER, A.E., 1963. Sulphur compounds in kraft pulp mill effluents. Can. Pulp Paper Ind., 16, 3, 35-43).<br><br>The tests were made in glass cylinders of 110 ml capacity.<br>Volume of test solution : 100 ml.<br>Temperature : About 20°C (test conducted at room temperature).<br><br>Conditions : The water fleas were handled in a manner that no air could penetrate beneath their back shell during transfer.<br><br>Concentrations: The dilutions required were made in such a way that the test-animals would not suddenly encounter higher concentrations than were desired. |
| <b>Reliability</b>     | : (4) not assignable<br>Documentation insufficient for assessment.  |
| 31.08.2005             | (32)  |

### 4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

|                        |                                     |
|------------------------|-------------------------------------|
| <b>Species</b>         | : Selenastrum capricornutum (Algae) |
| <b>Endpoint</b>        | : growth rate                       |
| <b>Exposure period</b> | : 96 hour(s)                        |

## 4. Ecotoxicity

Id 75-75-2

Date 10.10.2006

**Unit** : mg/l  
**NOEC** : = 5.8 measured/nominal  
**EC10** : = 2.1- 15 calculated  
**EC50** : = 7.2- 20 calculated  
**EC90** : = 12 - 26 calculated  
**EbC50** : = 8.6- 19 calculated  
**ErC50** : = 7.6- 24 calculated  
**Limit test** : no  
**Analytical monitoring** : yes  
**Method** : OECD Guide-line 201 "Algae, Growth Inhibition Test"  
**Year** : 1984  
**GLP** : yes  
**Test substance** :

**Result** : Measured concentrations were at least 87% of nominal concentrations.

Percent cell density; biomass; growth inhibition

2.7 mg/l (0.62%; -5.6%; -1.7%)

5.8 mg/l (5.4%; 7.0%; 0.38%)

12 mg/l (7.9%; 14%; 0.99%)

>24 mg/l (100%; 100%; 100%)

Percent cell density; biomass; growth inhibition when pH adjusted to 7.5

49 mg/l (0.62%; -5.6%; -1.6%)

95 mg/l (2.1%; 1.6%; -0.76%)

Based on cell density, the NOEC was determined to be 5.8 mg A.l./L. The 96-hour EC50, EC10 and EC90 were calculated to be 14, 8.8 and 19 mg A.l./L, respectively.

Based on total biomass, the NOEC was determined to be 5.8 mg A.l./L. The 0-72 hour EbC50 was calculated to be 14 (8.6-19) mg A.l./L.

Based on average growth rate, the NOEC was determined to be 12 mg A.l./L. The 0-72-hour ErC50 was calculated to be 16 (7.6-24) mg A.l./L.

**Source** : Atofina, Paris-la-Défense, France  
Atofina Paris La Défense Cedex

**Test condition** : TEST ORGANISMS  
- Strain: 1648, class Chlorophyceae.  
- Source/supplier: The alga was originally obtained from the University of Texas and maintained in stock culture.  
- Method of cultivation: The stock cultures were maintained within the following conditions: a shaking rate of 100+/-10 rpm, a temperature of 24+/-1°C and continuous illumination at the surface of the medium.  
- Pretreatment: the inoculum used to initiate the toxicity test with methane sulfonic acid was taken from a stock culture that had been transferred to fresh medium three days before testing.  
- Initial cell concentration: 10000 cells/ml.

STOCK AND TEST SOLUTION AND THEIR PREPARATION

- Dispersion: The 100 mg A.l.(active ingredient)/L test solution was prepared by adding 0.4267 g of methane sulfonic acid to 3000-ml of AAP medium. The resulting test solution was clear, no visible signs of undissolved test substance.

STABILITY OF THE TEST CHEMICAL SOLUTIONS: No data.

## DILUTION WATER

Algal assay procedure (AAP) medium.  
GROWTH/TEST MEDIUM CHEMISTRY

NaNO<sub>3</sub> : 25.5 mg/l

MgCl<sub>2</sub>.6H<sub>2</sub>O : 12.16 mg/l

CaCl<sub>2</sub>.2H<sub>2</sub>O : 4.41 mg/l

MgSO<sub>4</sub>.7H<sub>2</sub>O : 14.7 mg/l

K<sub>2</sub>HPO<sub>4</sub>.3H<sub>2</sub>O : 1.368 mg/l

NaHCO<sub>3</sub> : 15 mg/l

H<sub>3</sub>BO<sub>3</sub> : 185.5 µg/l

Na<sub>2</sub>SeO<sub>4</sub> : 1.88 µg/l

MnCl<sub>2</sub>.4H<sub>2</sub>O : 415.4 µg/l

ZnCl<sub>2</sub> : 3.270 µg/L

CoCl<sub>2</sub>.6H<sub>2</sub>O : 1.43 µg/l

CuCl<sub>2</sub>.2H<sub>2</sub>O : 0.012 Mg/l

Na<sub>2</sub>MoO<sub>4</sub>.2H<sub>2</sub>O : 7.26 µg/L

FeCl<sub>3</sub>.6H<sub>2</sub>O : 159.8 Mg/L

Na<sub>2</sub>EDTA.2H<sub>2</sub>O : 300 Mg/L

- pH: The pH of the culture medium was adjusted, if necessary, to pH 7.5+/-0.1 with either 0.10 N HCl or 0.10N NaOH.

## TEST SYSTEM

- Test type: The test was conducted in an environmental chamber (adjusted to maintain the test conditions) with an orbital shaker table.

- Renewal of test solution: no.

- Exposure vessel type: Replicate sterile 250-ml Erlenmeyer flasks were conditioned prior to use by rinsing with the appropriate exposure solution. All test vessels were fitted with stainless steel caps to permit gas exchange.

- Number of replicates: 3.

- Concentrations:

Nominal test concentration: 3.1, 6.3, 13, 25, 50, and 100 mg A.I./L; 50 and 100 mg A.I./L adjusted to pH 7.5.

Mean measured concentration: 2.7, 5.8, 12, 24, 47 and 96 mg A.I./L; 49 and 95 mg A.I./L respectively.

- Test temperature: 24+/-1°C.

- pH: From 7.6 to 7.5 at T<sub>0</sub> and 9.4 to 9.3 at 96 hours.

- Photoperiod: Continuous light intensity of 3200 to 5400 lux.

TEST PARAMETER: Inhibition of test density (inhibition of cell multiplication)

MONITORING OF TEST SUBSTANCE CONCENTRATION: Due to the acidic nature of the test solutions, two additional concentrations, 50 and 100 mg A.I./L were adjusted to pH 7.5 and tested in addition to the above concentrations.

**Test substance** : Test substance: methanesulfonic acid  
CAS no.: 75-75-2  
Source: Atochem  
Batch number: 2324E20HD1  
Purity: 70.3% in water.

**Attached document** : 75-75-2 5.bmp



- Conclusion** : Based on the results of definitive test, it is evident that the acidic nature of the test substance contributed to the toxicity observed. Additionally, the inhibition of algal growth in the acidic medium at a nominal concentration of 25 mg A.I./L was reversible once diluted to a nontoxic pH.
- Cell densities in the 49 and 95 mg A.I./L solutions which were adjusted to pH 7.5 were similar to that of the control. This data indicates that the acidic nature of the non-pH adjusted test solutions was probably the cause of algal inhibition in the definitive test.
- The results of the recovery phase indicated that the effects of Methane sulfonic acid on algal growth were algistatic rather than algicidal.
- Reliability Flag** : (1) valid without restriction  
: Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint
- 31.08.2005 (24)

#### 4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

- Type** : other: activated sludge  
**Species** : activated sludge of a predominantly domestic sewage  
**Exposure period** : 3 hour(s)  
**Unit** : mg/l  
**EC50** : = 530  
**Analytical monitoring** : no  
**Method** : ISO 8192 "Test for inhibition of oxygen consumption by activated sludge"  
**Year** : 1986  
**GLP** : no  
**Test substance** :
- Method** : Analytical device: Jenway 3410 (oxymeter, conductimeter, pH-meter)  
**Remark** : Study peer reviewed  
**Result** : See Attached Document 2
- At the highest concentration (1000 mg/l) methane sulfonic acid exhibited a 76.2% inhibiting effect on activated sludge respiration after a 3-hour exposition.
- The lowest tested concentration (100 mg/l) did not reveal any inhibiting effect (1.2%).
- Source** : Atofina, Paris-la-Défense, France  
 Atofina Paris La Défense Cedex  
**Test condition** : TEST ORGANISMS  
 - Source/supplier: Versailles water waste treatment plant  
 - Laboratory culture: activated sludge is sampled then its suspended particles are titrated (result: 1.8 g/l). After centrifugation, supernatant is discarded and residue is resuspended in an isotonic medium mixed with synthetic

medium (3:100 v/v) in order to have a 1.5 g/l final concentration in test flasks.

- Method of cultivation: no data
- Plate composition: no data
- Pretreatment: no data

#### STOCK AND TEST SOLUTION AND THEIR PREPARATION

- Dispersion: a stock solution of 5 g/l methane sulfonic acid is prepared, then properly diluted (cf. Attached Document 1)
- Vehicle, solvent: ultrafiltered water

STABILITY OF THE TEST CHEMICAL SOLUTIONS: No data

REFERENCE SUBSTANCE: 3,5-dichlorophenol

#### DILUTION WATER

- Source: no data
- Aeration: yes

#### GROWTH TEST MEDIUM CHEMISTRY

. Synthetic medium:  
 Peptone: 16 g  
 Meat extract: 11 g  
 Urea: 3 g  
 NaCl: 0.7 g  
 CaCl<sub>2</sub>, 2H<sub>2</sub>O: 0.4 g  
 MgSO<sub>4</sub>, 7H<sub>2</sub>O: 0.2 g  
 K<sub>2</sub>HPO<sub>4</sub>: 2.8 g  
 Ultra-pure water: qsp 1000 ml

. Isotonic solution:  
 NaCl: 5 g  
 MgSO<sub>4</sub>, 7H<sub>2</sub>O: 0.12g  
 Ultra-pure water: qsp 1000 ml

- pH: 7.5 ± 0.5

#### TEST SYSTEM

- Exposure vessel type: 1 litre Erlenmeyer flasks
- Microorganism initial concentration: 1.5 g/l
- Exposure schedule: after 3 hours incubation, oxygen is measured every minute for approximately 10 minutes, until oxygen concentration reaches 1 mg/l
- Number of replicates per dose: 1
- Concentrations: 100, 180, 320, 580 and 1000 mg/l
- Control: vehicle
- Test temperature: 18.6 to 19.1°C
- Photoperiod: no data

TEST PARAMETER: Oxygen is measured in each test and control flask.

MONITORING OF TEST SUBSTANCE CONCENTRATION: no data

#### Test substance

: Test substance: methanesulfonic acid  
 C AS no.: 75-75-2  
 Source: Elf Atochem  
 Batch number: 2690  
 Purity: 70% in water

#### Attached document

: 75-75-2 Sludge respiration inhibition (dose table).bmp  
 75-75-2 Sludge respiration inhibition (results table).bmp

**Conclusion** : Methane sulfonic acid exhibit an inhibiting effect on oxygen consumption of microorganisms contained in activated sludge of a waste water treatment plant. In the experimental conditions of this study, methane sulfonic acid presents a EC50-3h of 530 mg/l.

**Reliability** : No physico-chemical oxygen consumption has been noticed.  
**Flag** : (2) valid with restrictions  
 02.01.2006 : Material Safety Dataset, Directive 67/548/EEC

(15)

**Type** : other  
**Species** : Pseudomonas putida (Bacteria)  
**Exposure period** : 16 hour(s)  
**Unit** : mg/l  
**EC0** : calculated  
**EC10** : = .54 calculated  
**EC50** : = 1.8  
**Analytical monitoring** : no data  
**Method** : other: ISO 10712  
**Year** :  
**GLP** : no  
**Test substance** :

**Method** : Analytical device: Perkin-Elmer lambda 5 spectrometer  
 Data treatment: Probit's method

**Remark** : Study peer reviewed  
**Result** : Test substance results:  
 See attached document.

Reference substance results:  
 EC10 and EC50 of 3,5-dichlorophenol were respectively 8.1 and 13 mg/l.

**Source** :  
**Test condition** :  
 Validity criterion:  
 Control growth factor = 218 (>60)  
 : Atofina Paris La Défense Cedex  
 : TEST ORGANISMS  
 - Source/supplier: Institut Pasteur 103281  
 - Laboratory culture: no data  
 - Method of cultivation: no data  
 - Plate composition: no data  
 - Pretreatment: no data

STOCK AND TEST SOLUTION AND THEIR PREPARATION  
 - Dispersion: no data

- Vehicle, solvent: test medium

STABILITY OF THE TEST CHEMICAL SOLUTIONS: No data

REFERENCE SUBSTANCE: 3,5-dichlorophenol

DILUTION WATER

- Source: no data  
- Aeration: no data

GROWTH TEST MEDIUM CHEMISTRY

- no data  
- pH: 3.25 to 4.01

TEST SYSTEM

- Exposure vessel type: no data  
- Microorganism initial concentration: no data  
- Exposure schedule: no data  
- Number of replicates per dose: 3  
- Concentrations: 0.25, 0.50, 1, 2, 4 and 8 mg/l  
- Control: vehicle  
- Test temperature: 21 ± 1°C  
- Photoperiod: no data

TEST PARAMETER: turbidity is measured by a spectrophotometer at 436 nm

MONITORING OF TEST SUBSTANCE CONCENTRATION: no data

**Test substance**

: Test substance: methanesulfonic acid  
C AS no.: 75-75-2  
Source: Elf Atochem  
Batch number: no data  
Purity: no data

**Conclusion**

: Growth inhibition test was performed on *Pseudomonas putida* for 16 hours. Inhibition was assessed by a turbidimetric comparison between test and control cultures. Results were found as follows:  
EC50 = 1.8 mg/l (IC95%: 1.2-2.6)  
EC10 = 0.54 mg/l (IC95%: 0.23-0.85)

**Reliability**

: (2) valid with restrictions

**Flag**

: Material Safety Dataset, Directive 67/548/EEC

02.01.2006

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#### 4.5.1 CHRONIC TOXICITY TO FISH

#### 4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

#### 4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

#### 4.6.2 TOXICITY TO TERRESTRIAL PLANTS

#### 4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

### 4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

**Species** : other avian: Agelaius phoeniceus  
**Endpoint** : mortality  
**Exposure period** :  
**Unit** : mg/kg bw  
**LC50** : > 100  
**Method** : other  
**Year** :  
**GLP** :  
**Test substance** :

**Source** : Atofina, Paris-la-Défense, France  
Atofina Paris La Défense Cedex  
**Reliability** : (4) not assignable  
Collection of data

31.08.2005

(38)

### 4.7 BIOLOGICAL EFFECTS MONITORING

### 4.8 BIOTRANSFORMATION AND KINETICS

**Source** : Atofina Paris La Défense Cedex  
27.12.2002

### 4.9 ADDITIONAL REMARKS

## 5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

## 5.1.1 ACUTE ORAL TOXICITY

**Type** : LD50  
**Value** : = 649 mg/kg bw  
**Species** : rat  
**Strain** : Sprague-Dawley  
**Sex** : male/female  
**Number of animals** : 30  
**Vehicle** : other: undiluted  
**Doses** : 300, 500 and 750 mg/kg  
**Method** : other: EPA 40 CFR Part 792  
**Year** :  
**GLP** : yes  
**Test substance** :

**Result** : MORTALITY:

## CLINICAL SIGNS:

The majority of clinical abnormalities were observed in both the animals that died and those that survived to day 14 and included salivation, decreased activity, wobbly gait, breathing abnormalities, apparent hypothermia, decreased/no defecation, feces small in size, urine stain, hunched posture, unkempt appearance, rough haircoat, piloerection, extremities pale in color, dehydration, emaciation, distended abdomen, decreased food consumption and dark material around the facial area.

## BODY WEIGHT:

Body weight loss was noted for one 300 mg/kg male, one 500 mg/kg male, two 500 mg/kg females and one 750 mg/kg male during the study day 0-7 body weight interval. Body weight loss was noted for one 300 mg/kg male and one 750 mg/kg male during the study day 7-14 body weight interval. Body weight gain was noted for all other surviving animals during the test period.

## NECROPSY FINDINGS:

Gross internal findings observed in the animals that died included distension/abnormal content/reddened mucosa in the digestive tract, dark red/mottled lungs, blackish-purple spleens, dark red lymph nodes, stained glandular mucosa in the stomach and body fat depletion/dyscoloration/adhesions in the abdominal cavity. Gross internal findings observed at necropsy on study day 14 included abnormal content in the digestive tract and thickened mucosa in the stomach.

## POTENTIAL TARGET ORGANS:

no specific target-organs were detected

## SEX-SPECIFIC DIFFERENCES:

Male LD50 > 750 mg/kg  
 Female LD50 = 461.2 mg/kg (IC95%: 313.3 - 679.0)

**Source** : ATOFINA, Paris-La Défense, France.  
 Atofina Paris La Défense Cedex

**Test condition** : TEST ORGANISMS:

## 5. Toxicity

Id 75-75-2

Date 10.10.2006

- Source: Charles River Laboratories, Inc., Portage, Michigan.
- Age: no data
- Weight at study initiation: 200 to 300 g
- Number of animals: 5 males + 5 females / dose
- Controls: no
- Other:

### HOUSING

The animals were housed individually in suspended stainless steel cages

### FOOD and WATER

- Food: PMI certified rodent chow # 5002t ad libitum
- Water: filtered tap water ad libitum

### ENVIRONMENTAL CONDITIONS

- Temperature : 64-70°F
- Relative humidity : 40-54%
- Light/dark cycle : 12h/12h
- Ventilation : about 10-15 cycles/hour

### ADMINISTRATION:

- Exposure route: gavage
- Volume administered: 0.21-0.54 ml test article/kg
- Post dose observation period: 14 days

EXAMINATIONS: clinical observations, body weight and necropsy

- Test substance** : Test substance: anhydrous methanesulfonic acid  
CAS no.: 75-75-2  
Source: Elf Atochem  
Batch number: 2690J24HS1  
Purity: 99.6%
- Conclusion** : The acute oral LD50 of Methane Sulfonic Acid, Anhydrous in the male rat was estimated to be greater than 750 mg/kg. In the female rat, the acute oral LD50 was determined to be 461 mg/kg. In the sexes combined, the acute oral LD50 was determined to be 649 mg/kg (IC95%: 380.8-1105.1 mg/kg).
- Reliability Flag** : (1) valid without restriction  
: Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint

16.08.2005

(16)

- Type** : LD50  
**Value** : = 1157 mg/kg bw  
**Species** : rat  
**Strain** : Sprague-Dawley  
**Sex** : male/female  
**Number of animals** : 30  
**Vehicle** : water  
**Doses** : 500, 1000, 1500 mg/kg  
**Method** : other: EPA 40 CFR Part 792  
**Year** :  
**GLP** : yes  
**Test substance** :

- Method** : Statistical test: LD50 was determined separately for both sexes, using Litchfield and Wilcoxon method.

- Result** : CLINICAL SIGNS:  
The most notable clinical abnormalities observed during the study included salivation, breathing abnormalities, wobbly

gait, decreased activity, decreased defecation, rough haircoat, urine/fecal stain and dark material around the facial area.

#### BODY WEIGHT:

Body weight loss was noted for one 1000 mg/kg male and one 1000 mg/kg female during the study day 0-7 body weight interval and for one 300 mg/kg male and one 1000 mg/kg male during the study day 7-14 body weight interval. Body weight gain was noted for all other surviving animals during the test period.

#### NECROPSY FINDINGS:

The most notable gross internal findings were observed in the animals that died and included abnormal content and reddened/thickened mucosa and discoloration in the digestive tract, dark red foci on the liver and blackish-purple spleens. No significant gross findings were observed at necropsy on day 14.

#### POTENTIAL TARGET ORGANS:

Digestive tract

#### SEX-SPECIFIC DIFFERENCES:

Male LD50 = 860.1 mg/kg (IC95%: 540.1 - 1369.7)

Female LD50 = 2407.6 mg/kg (IC95%: 944.2- 6139.2).

#### Source

: ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex

#### Test condition

: TEST ORGANISMS:  
- Source: Charles River Laboratories, Inc., Portage, Michigan.  
- Age: no data  
- Weight at study initiation: 205,3 g (males) and 204.7 g (females)  
- Number of animals: 5 males + 5 females / dose  
- Controls: no

#### HOUSING

The animals were housed individually in suspended stainless steel cages

#### FOOD and WATER

- Food: PMI certified rodent chow # 5002t ad libitum  
- Water: filtered tap water ad libitum

#### ENVIRONMENTAL CONDITIONS

- Temperature : 68-76°F  
- Relative humidity : 38-61%  
- Light/dark cycle : 12h/12h  
- Ventilation : about 10-15 cycles/hour

#### ADMINISTRATION:

- Exposure route: gavage  
- Volume administered: 0.38, 0.75 and 1.13 ml/kg  
- Post dose observation period: 14 days

EXAMINATIONS: clinical observations, body weight, mortality and necropsy

#### Test substance

: Test substance: methanesulfonic acid  
CAS no.: 75-75-2  
Source: Elf Atochem  
Batch number: D11HD1

|   |  |
|---|--|
| <b>Conclusion</b>   | <p>Purity: 70% in water</p> <p>: The acute oral LD50 of 70% METHANE SULFONIC ACID in the male rat was determined to be 860.1 mg/kg (IC95%: 540.1 -1369.7). In the female rat, the oral LD50 was determined to be 2407.6 mg/kg (IC95%: 944.2 -6139.2). Nothing explains such a sex-difference.</p> <p>In the sex combined, the oral LD50 was valued at 1157.5 mg/kg (IC50%: 748.0 -1791.0).</p> <p>PS: previous data are expressed in mg of tested solution (diluted at 70%). Results in terms of active substance can be obtained by multiplication by 0.7, as follows:<br/> Males LD50: 602.07 mg/kg (IC95%: 378.07-958.79)<br/> Females LD50: 1685.32 mg/kg (IC95%: 660.94-4297.44)<br/> Global LD50: 810.25 mg/kg (IC95%: 523.6 -1253.77)</p>         |
| <b>Reliability Flag</b>   | <p>: (1) valid without restriction</p> <p>: Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint</p>  |
| 30.08.2005  | (17)   |
| <b>Type Value Species Strain Sex Number of animals Vehicle Doses Method Year GLP Test substance</b> | <p>: LD50</p> <p>: = .281 ml/kg bw</p> <p>: rat</p> <p>: Wistar</p> <p>: male</p> <p>: 28</p> <p>: other: undiluted</p> <p>: 0.25, 0.5 and 1.0 ml/kg</p> <p>: other: unprecised EPA guidance</p> <p>: 1975</p> <p>: no</p> <p>:</p>  |
| <b>Result</b>   | <p>: CLINICAL OBSERVATIONS:</p> <p>At 0.25 ml/kg, rats were sluggish and presented an unsteady gait.</p> <p>At 0.5 ml/kg, they exhibited the same symptoms as above. Death occurred within 40 minutes.</p> <p>At 1.0 ml/kg, sluggish and unsteady gait were noted. Deep breathing was immediately observed.</p> <p>MORTALITY:</p> <p>At 0.25 ml/kg, 2 rats (among 5) died within 40 minutes.</p> <p>At 0.5 ml/kg, all rats died (2 on first day, 2 on second day and 1 on fifth day)</p> <p>At 1.0 ml/kg, 2 rats (among 3) died within 45 minutes.</p> <p>NECROPSY:</p> <p>Livers mottled and burned, stomach burned, pylorus haemorrhaged and gas filled, intestines haemorrhaged, injected and gas filled, kidneys mottled and slightly congested.</p> |
| <b>Source</b>   | <p>LD50: 0.281 ml/kg (0.146-0.540)</p> <p>: ATOFINA, Paris-La Défense, France.<br/> Atofina Paris La Défense Cedex</p>   |
| <b>Test condition</b>   | <p>: TEST ORGANISMS:</p> <p>- Source: Harlan Industries, Cumberland.</p> <p>- Age: 30 days</p> <p>- Weight at study initiation: ca. 80</p> <p>- Number of animals: 5 rats / dose (except 3 rats at the higher dose)</p>  |

## 5. Toxicity

Id 75-75-2  
Date 10.10.2006

- Controls: no

ADMINISTRATION:  
- Exposure route: gavage  
- Volume administered: no data  
- Post dose observation period: no data

EXAMINATIONS: clinical observations, mortality and necropsy

**Test substance** : Test substances: Methane sulfonic acid  
CAS no.: 75-75-2  
Source: South Charleston, WV.  
Batch number: 38-119  
Purity: 98% (anhydrous grade)

**Reliability** : (2) valid with restrictions (43)  
17.03.2006

**Type** : LD50  
**Value** : ca. 200 - 400 mg/kg bw  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Doses** :  
**Method** : other  
**Year** :  
**GLP** : no  
**Test substance** : no data

**Source** : ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex

**Reliability** : (4) not assignable  
documentation insufficient for assessment. (8)  
17.03.2006

**Type** : LD50  
**Value** : = 6170 mg/kg bw  
**Species** : rat  
**Strain** : Wistar  
**Sex** : male  
**Number of animals** : 13  
**Vehicle** : water  
**Doses** : 2000, 4000 and 8000 mg/kg  
**Method** : other: unprecised EPA guidance  
**Year** :  
**GLP** : no  
**Test substance** :

**Result** : CLINICAL OBSERVATIONS:  
At 2000 mg/kg: no symptoms  
At 4000 mg/kg: sluggish behavior  
At 8000 mg/kg: sluggish gait and pilo-erection.

MORTALITY:  
At 2000 mg/kg: no death  
At 4000 mg/kg: no death  
At 8000 mg/kg: 4 rats (among 5) died: 3 on first day and 1 on second day.

NECROPSY:

## 5. Toxicity

Id 75-75-2

Date 10.10.2006

|                                  |   |
|----------------------------------|---|
|                                  | Livers and spleens mottled, kidneys speckled and slightly congested, stomachs and intestines distended and liquid filled.   |
| <b>Source</b>                    | : LD50: 6170 (4570-8330) mg/kg<br>: ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex  |
| <b>Test condition</b>            | : TEST ORGANISMS:<br>- Source: Harlan Industries, Cumberland.<br>- Age: 30 days<br>- Weight at study initiation: ca. 80<br>- Number of animals: 5 rats / dose (except 3 rats at the lower dose)<br>- Controls: no           |
|                                  | ADMINISTRATION:<br>- Exposure route: gavage<br>- Volume administered: no data<br>- Post dose observation period: no data  |
| <b>Test substance</b>            | : EXAMINATIONS: clinical observations, mortality and necropsy<br>: Test substances: Methane sulfonic acid, potassium salt<br>CAS no.: 2386-56-3<br>Source: South Charleston, WV.<br>Batch number: 38-263<br>Purity: no data |
| <b>Reliability</b><br>30.08.2005 | : (2) valid with restrictions   |

(43)

### 5.1.2 ACUTE INHALATION TOXICITY

|                          |   |
|--------------------------|---|
| <b>Type</b>              | : LC0   |
| <b>Value</b>             | : > .05 mg/l  |
| <b>Species</b>           | : mouse   |
| <b>Strain</b>            | : no data   |
| <b>Sex</b>               | : male  |
| <b>Number of animals</b> | : 5   |
| <b>Vehicle</b>           | : no data   |
| <b>Doses</b>             | : saturated atmosphere (estimated to be about 0.05 mg/l taking into account a vapor pressure of 0.13 hPa at 20°C)   |
| <b>Exposure time</b>     | : 1 hour(s)   |
| <b>Method</b>            | : other   |
| <b>Year</b>              | : 1976  |
| <b>GLP</b>               | : no  |
| <b>Test substance</b>    | :   |
| <b>Result</b>            | : No effects of any kind were discernible in any of the twenty mice either during or after exposure for 1 hour to saturated vapor at 20°C. All showed normal gains in body weight during the subsequent 7-day observation period. |
| <b>Source</b>            | : ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex  |
| <b>Test condition</b>    | : Test substance: Methanesulfonic acid<br>CAS no.: 75-75-2<br>Purity: no data   |
| <b>Test substance</b>    | : TEST ORGANISMS:<br>- Source: no data<br>- Age: no data<br>- Weight at study initiation: 32 g<br>- Number of animals: (per sex and dose)   |

|                          |   |      |
|--------------------------|---|------|
|                          | - Controls: no  |      |
|                          | ADMINISTRATION:   |      |
|                          | - Type of exposure: whole body  |      |
|                          | - Other: Atmospheric saturation was obtained by placing 2 g of the sample in an airtight twenty-litre chamber and allowing 24h for evaporation. |      |
|                          | The chamber was then momentarily opened to permit the quick insertion of mice.  |      |
|                          | EXAMINATIONS: clinical observations and body weight.  |      |
| <b>Conclusion</b>        | : Insufficient volatility of methane sulfonic acid limits the actual exposure and therefore toxicity risks.                                     |      |
| <b>Reliability</b>       | : (2) valid with restrictions<br>Lack of information about the method.  |      |
| <b>Flag</b>              | : Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint   |      |
| 17.03.2006               |   | (34) |
| <b>Type</b>              | : LCO   |      |
| <b>Value</b>             | :   |      |
| <b>Species</b>           | : rat   |      |
| <b>Strain</b>            | : no data   |      |
| <b>Sex</b>               | : no data   |      |
| <b>Number of animals</b> | :   |      |
| <b>Vehicle</b>           | :   |      |
| <b>Doses</b>             | :   |      |
| <b>Exposure time</b>     | : 6 hour(s)   |      |
| <b>Method</b>            | : other   |      |
| <b>Year</b>              | :   |      |
| <b>GLP</b>               | : no  |      |
| <b>Test substance</b>    | : no data   |      |
| <b>Remark</b>            | : No effect in rats after 6 hours of inhaling vapor from heated liquid.   |      |
| <b>Source</b>            | : ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex  |      |
| <b>Reliability</b>       | : (4) not assignable<br>documentation insufficient for assessment.  |      |
| 17.03.2006               |   | (9)  |

### 5.1.3 ACUTE DERMAL TOXICITY

|                          |   |
|--------------------------|---|
| <b>Type</b>              | : LD0   |
| <b>Value</b>             | : > 1000 mg/kg bw   |
| <b>Species</b>           | : rabbit  |
| <b>Strain</b>            | : New Zealand white   |
| <b>Sex</b>               | : male/female   |
| <b>Number of animals</b> | : 10  |
| <b>Vehicle</b>           | : water   |
| <b>Doses</b>             | : 1000 mg/kg  |
| <b>Method</b>            | : OECD Guide-line 402 "Acute dermal Toxicity"   |
| <b>Year</b>              | :   |
| <b>GLP</b>               | : yes   |
| <b>Test substance</b>    | :   |
| <b>Method</b>            | : Initially, one healthy male New Zealand White rabbit was dosed dermally at 1000 mg/kg of Methane Sulfonic Acid (MSA) (test sample of 70% MSA in water was diluted to yield 200 mg MSA/ml, dose volume was 5 ml/kg). Since no irritation was |

|                         |  |
|-------------------------|--|
| <b>Result</b>           | <p>noted, an additional nine animals (4 males and 5 females) were dosed. The test article was kept in contact with the skin for 24 hours. Dermal responses were recorded 24 hours postdose and on days 7 and 14. Animals were observed for mortality, toxicity and pharmacological effects at 1 and 2 hours postdose and once daily for 14 days. Body weights were recorded pretest and at termination. All animals were examined for gross pathology.</p> <p>: All animals survived the dermal application of 1000 mg/kg Methane Sulfonic Acid.</p> <p>Instances of few feces were the only abnormal physical signs noted during the observation period.</p> <p>Dermal responses were slight to well defined on day 1, absent to severe on day 7 and absent to slight on day 14. Body weight changes were normal.</p>   |
| <b>Source</b>           | <p>Necropsy results were normal.</p> <p>: Atofina, Paris-La-Defense, France<br/>Atofina Paris La Défense Cedex</p>   |
| <b>Test condition</b>   | <p>: TEST ORGANISMS:</p> <ul style="list-style-type: none"> <li>- Source: Millbrook Breeding Labs, Amherst MA</li> <li>- Age: ca. 10 weeks</li> <li>- Weight at study initiation: 2.5-3.1 kg for males, 2.8-3.0 kg for females</li> <li>- Number of animals: 5 males + 5 females / dose</li> <li>- Controls: no</li> <li>- Acclimatation: at least one week</li> </ul> <p>HOUSING</p> <p>The animals were housed individually in suspended wire cages</p> <p>FOOD and WATER</p> <ul style="list-style-type: none"> <li>- Food: PMI rabbit chow #5321 ad libitum</li> <li>- Water: tap water ad libitum</li> </ul> <p>ENVIRONMENTAL CONDITIONS</p> <ul style="list-style-type: none"> <li>- Temperature : no data</li> <li>- Relative humidity : no data</li> <li>- Light/dark cycle : 12h/12h</li> <li>- Ventilation : no data</li> </ul> <p>ADMINISTRATION:</p> <ul style="list-style-type: none"> <li>- Exposure route: occlusive dermal</li> <li>- Concentration of the test solution: 200 mg/ml</li> <li>- Volume administered: not specified (probably 5 ml/kg to achieve a dose of 1000 mg/kg)</li> <li>- Post dose observation period: 14 days</li> </ul> |
| <b>Test substance</b>   | <p>EXAMINATIONS: clinical observations, dermal irritation, body weight and necropsy</p> <p>: Test substance: Methanesulfonic acid<br/>C AS no.: 75-75-2<br/>Source: Atofina Chemicals Inc<br/>Purity: 70.2% in water</p>   |
| <b>Conclusion</b>       | <p>: The LD0 of Methane Sulfonic Acid is greater than 1000 mg/kg of body weight.</p>   |
| <b>Reliability Flag</b> | <p>: (1) valid without restriction</p> <p>: Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint</p>  |

17.03.2006

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## 5. Toxicity

Id 75-75-2

Date 10.10.2006

**Type** : LD50  
**Value** : ca. 200 - 2000 mg/kg bw  
**Species** : rabbit  
**Strain** : other: albino  
**Sex** : no data  
**Number of animals** : 6  
**Vehicle** : other: undiluted (2000 mg/kg) and water (200 mg/kg)  
**Doses** : 200 and 2000 mg/kg  
**Method** : other  
**Year** : 1978  
**GLP** : no  
**Test substance** :

**Result** : At 2000 mg/kg:  
Skin contact caused intense and prolonged pain.  
At the end of exposure, the skin of each animal was dark grey in appearance and scattered portions were separating from the subcutaneous tissues.  
2 rabbits died the following night (28h after initial contact) and 1 rabbit was euthanized three days after treatment for humane reasons.

At 200 mg/kg : No mortality. Erythema (score 2) was present over the entire trunk of each animal together with numerous small lesions.  
Animals nevertheless remained asymptomatic and gained body weight during the observation period.

**Source** : ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex

**Test condition** : TEST ORGANISMS:  
- Source: no data  
- Age: no data  
- Weight at study initiation: no data  
- Number of animals: no data  
- Controls: no

ADMINISTRATION:  
- Area covered: no data  
- Exposure: pre-fitted impervious sleeve  
- Concentration in vehicle: undiluted or 10% (w/v)  
- Total volume applied: no data  
- Removal of test substance: with a saturated solution of sodium bicarbonate  
- Exposure duration: 24h  
- Post-dose observation period: 7 days

EXAMINATIONS: clinical observations and mortality

**Test substance** : Test substance: Methanesulfonic acid (anhydrous)  
CAS no.: 75-75-2  
Purity: no data

**Conclusion** : A 2000 mg/kg dermal exposure to methane sulfonic acid is highly toxic (severe skin injuries causing death) whereas 200 mg/kg exposure induces minor skin lesions (erythema) but no systemic toxicity.

**Reliability** : (2) valid with restrictions  
Details on the protocol used are not available.

**Flag** : Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint

17.03.2006

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## 5. Toxicity

**Id** 75-75-2  
**Date** 10.10.2006

**Type** : LD50  
**Value** : > 2000 mg/kg bw  
**Species** : guinea pig  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Doses** :  
**Method** : other: no data  
**Year** :  
**GLP** : no  
**Test substance** :  
  
**Remark** : LD50 > 20 ml/kg (of the 10% solution in water)  
Study peer reviewed  
**Source** : Atofina, Paris-La Défense, France.  
Atofina Paris La Défense Cedex  
**Test substance** : 10% MSA in water.  
**Reliability** : (4) not assignable  
Documentation insufficient for assessment.  
  
30.08.2005 (9)

### 5.1.4 ACUTE TOXICITY, OTHER ROUTES

**Type** : LC50  
**Value** : < 50 mg/kg bw  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Doses** :  
**Route of admin.** : i.p.  
**Exposure time** :  
**Method** : no data  
**Year** :  
**GLP** : no  
**Test substance** : no data  
**Source** : ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex  
**Reliability** : (4) not assignable  
Documentation insufficient for assessment.  
  
17.03.2006 (9)

### 5.2.1 SKIN IRRITATION

**Species** : mouse  
**Concentration** : undiluted  
**Exposure** : Open  
**Exposure time** : 1 hour(s)  
**Number of animals** : 4  
**Vehicle** :  
**PDII** :  
**Result** : corrosive  
**Classification** : corrosive (causes burns)  
**Method** : other: mouse tail method  
**Year** :  
**GLP** : no

## 5. Toxicity

Id 75-75-2

Date 10.10.2006

**Test substance** :

**Method** : The tails of four anesthetized mice were immersed in MSA to a depth of 4 cm. One hour later the tissue reaction was terminated by plunging the appendages into a saturated solution of sodium bicarbonate for a period of 30 seconds.

**Result** : The tail of each mouse was white when exposure was terminated and the appendage fell off in a day or two.

**Source** : ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex

**Test substance** : Test substance: Methanesulfonic acid anhydrous  
CAS no.: 75-75-2  
Source: Penwalt corporation  
Purity: no data

**Reliability** : (2) valid with restrictions

**Flag** : Material Safety Dataset, Directive 67/548/EEC  
17.03.2006 (34)

**Species** : other: in vitro Corrositex method (see section 5.9)

**Concentration** :

**Exposure** :

**Exposure time** :

**Number of animals** :

**Vehicle** :

**PDII** :

**Result** :

**Classification** :

**Method** :

**Year** :

**GLP** :

**Test substance** :

**Source** : Atofina Paris La Défense Cedex  
16.08.2005

### 5.2.2 EYE IRRITATION

**Species** : rabbit

**Concentration** : undiluted

**Dose** : .1 ml

**Exposure time** :

**Comment** : other: one of the two animals had a rinse of the treated eye

**Number of animals** : 2

**Vehicle** : none

**Result** : corrosive

**Classification** : risk of serious damage to eyes

**Method** : other

**Year** : 1978

**GLP** : no

**Test substance** : as prescribed by 1.1 - 1.4

**Result** : Symptoms of pain (vocalization) were noted following each instillation.

Unwashed eye:  
The reaction involved all ocular tissues and occurred immediately.  
The conjunctivae became completely necrotic (white) without evident swelling.  
The iris was dilated with ragged edges and failed to react

|                           |   |   |
|---------------------------|---|---|
|                           |   | to light.<br>The cornea opacified completely within 24 hours.   |
|                           |   | Washed eye:<br>The reaction did not differ significantly from that of unwashed eye.   |
| <b>Source</b>             | : | ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex  |
| <b>Test condition</b>     | : | TEST ORGANISMS:<br>- Strain: Albino<br>- Sex: no data<br>- Source: no data<br>- Age: no data<br>- Weight at study initiation: no data<br>- Controls: auto-control   |
|                           |   | ADMINISTRATION:<br>- Administration frequency: single administration<br>- Other: one of the two animals had a rinse of the treated eye with flowing water (initiated 20 to 30 seconds after instillation and continued for one minute). |
|                           |   | EXAMINATIONS:<br>- Ophthalmoscopic examination: Yes<br>- Scoring system: not mentioned<br>- Observation period: 10 min, 1h, 2h, 3h, 4h, 24h, 48h, 72h, 4 days, 5 days, 6 days and 7 days.<br>- Tool used to assess score: no data       |
| <b>Test substance</b>     | : | Test substance: Methanesulfonic acid (anhydrous)<br>C AS no.: 75-75-2<br>Source: Penwalt corporation<br>Purity: no data   |
| <b>Conclusion</b>         | : | Methane sulfonic acid is extremely corrosive to eye.  |
| <b>Reliability</b>        | : | (2) valid with restrictions<br>Even if method used differs from guidelines, corrosivity of methane sulfonic acid is evidently highlighted and does not require additional animal testing.   |
| <b>Flag</b><br>17.03.2006 | : | Material Safety Dataset, Directive 67/548/EEC   |

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### 5.3 SENSITIZATION

|                          |   |   |
|--------------------------|---|---|
| <b>Type</b>              | : | other: Buehler derived test   |
| <b>Species</b>           | : | guinea pig  |
| <b>Concentration</b>     | : | 1 <sup>st</sup> : Induction 50 % occlusive epicutaneous<br>2 <sup>nd</sup> : Challenge 25 % occlusive epicutaneous<br>3 <sup>rd</sup> :   |
| <b>Number of animals</b> | : | 30  |
| <b>Vehicle</b>           | : | water   |
| <b>Result</b>            | : | not sensitizing   |
| <b>Classification</b>    | : | not sensitizing   |
| <b>Method</b>            | : | other: not mentionned   |
| <b>Year</b>              | : |   |
| <b>GLP</b>               | : | yes   |
| <b>Test substance</b>    | : | other TS  |
| <b>Result</b>            | : | RESULTS OF PILOT STUDY:<br>Undiluted methane sulfonic acid 70% produced grades of 2, 1 and ±, with oedema, blanching and scabbing on two sites.<br>50%, 25%, 10%, 5%, 2.5% and 1% produced grades of ±, while |

0.5% produced grades of  $\pm$  and 0.  
Consequently, the 50% concentration was chosen for use at induction for the test group, since it caused no greater than mild to moderate primary irritation. Moreover, the 25% concentration was selected for challenge, because it caused no more than slight irritation.

#### RESULTS OF TEST

- Sensitization reaction: None of the test animals responded with a skin grade that would have been suggestive of sensitization.

- Clinical signs: no data

**Source** : ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex

**Test condition** : TEST ORGANISMS:

- Strain: Hartley

- Sex: male and female

- Source: Harlan Sprague Dawley (P.O. Box 29176, Indianapolis, Indiana 46229)

- Age: no data

- Weight at study initiation: 429.6  $\pm$  18.8 (males), 400.5  $\pm$  27.6g (females)

- Number of animals: 10 males + 10 females

- Controls: 5 males + 5 females

#### ADMINISTRATION:

- Induction schedule:

- On day 1, dermal application with 0.3 ml of test substance (treated group) or with the vehicle (control group) on the left shoulder.

- On day 7, the same region received another topical application

- On day 14, this same site was treated by a last topical application

All these applications lasted approximately 6 hours.

- Concentration in Freund's Complete Adjuvant (FCA): not used here

- Challenge schedule: On day 28, all the animals received 0.3 ml of the test substance at the concentration of 25% in their right flank.

- Challenge exposure duration : 24h

- Rechallenge: no

- Positive control: no

- Other:

#### EXAMINATIONS:

- Examination schedule: 24h after each induction and challenge application.

- Grading system:

0: no reaction

$\pm$ : slight, patchy erythema

1: slight but confluent or moderate patchy erythema

2: moderate erythema

3: severe erythema with or without oedema.

- Pilot study: Yes

A preliminary study was conducted in order to determine the concentrations to be tested in the main study.

The irritation potential of methane sulfonic acid 70% at levels of undiluted, 50%, 25%, 10%, 5%, 2.5%, 1% and 0.5% was evaluated in two groups of four animals each. Four levels of test material were evaluated per animals.

Dilutions were obtained with distilled water (w/v).

|                         |   |  |
|-------------------------|---|--|
|                         |   | 0.3 ml of different solutions was applied into a 25 mm Hill Top Chamber, which were placed on animals clipped back for 6 hours. The day after, animals were depilated and two hours later, examined for irritation, according the previously described scale.  |
|                         |   | Another score was performed 40h after exposure.  |
| <b>Test substance</b>   | : | Test substance: Methanesulfonic acid<br>C AS no.: 75-75-2<br>Source: Elf Atochem NA<br>Batch number: M12E<br>Purity: 70.38% in water   |
| <b>Conclusion</b>       | : | 20 guinea-pigs were induced by 50% of methane sul fonic acid 70% solution (i.e. 35% of methane sulfonic acid) and challenged by 25% of methane sulfonic acid 70% solution (i.e. 17.5% of methane sulfonic acid).<br>None of the test animals responded with a skin grade that would have been suggestive of sensitization. |
| <b>Reliability Flag</b> | : | (1) valid without restriction<br>Material Safety Dataset, Directive 67/548/EEC   |
|                         |   | 17.03.2006   |

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#### 5.4 REPEATED DOSE TOXICITY

|                             |   |   |
|-----------------------------|---|---|
| <b>Type</b>                 | : |   |
| <b>Species</b>              | : | rat   |
| <b>Sex</b>                  | : | male/female   |
| <b>Strain</b>               | : | other: Albino   |
| <b>Route of admin.</b>      | : | inhalation: aerosol   |
| <b>Exposure period</b>      | : | 4 weeks   |
| <b>Frequency of treatm.</b> | : | 6 hours/day, 5 days/week  |
| <b>Post exposure period</b> | : | 2-week recovery period  |
| <b>Doses</b>                | : | 0.026, 0.073 and 0.242 mg/L   |
| <b>Control group</b>        | : | yes, concurrent vehicle   |
| <b>NOAEL</b>                | : | = .026 mg/l   |
| <b>Method</b>               | : | other: EPA 40 CFR 792   |
| <b>Year</b>                 | : |   |
| <b>GLP</b>                  | : | yes   |
| <b>Test substance</b>       | : | other TS  |
| <b>Method</b>               | : | - Analytical device:<br>Ion exchange chromatography, Intox Products particle size analyzer model 02-140/JB, Teflon 25-mm filter and Mettler AE240 electronic balance (for gravimetric determination).<br>- Statistical tests:<br>One-way analysis of variance followed by a Dunnett's test using a Digital MicroVAX 3400 computer "with appropriate programming".<br>Fisher's Exact test was involved for discontinuous (ordinal or descriptive) functional observation battery data.<br>Clinical laboratory values for leukocytes that occur at a low incidence (monocytes, eosinophils, basophils, unsegmented neutrophils) were not subjected to statistical analysis. |
| <b>Result</b>               | : | - Mortality:<br>During the exposure phase of the study, 4, 1, 1 and 5 animals in the control, low -, mid- and high-exposure groups, respectively, were found dead. All deaths were attributed to confinement in the restraint tubes and none of the deaths were considered related to exposure to the test article. All other animals survived to the scheduled necropsies.   |

## - Clinical signs:

Exposure-related clinical signs consisted of rales in the high-exposure group animals and an increased incidence of yellow matting on various body surfaces in the mid-exposure group males and the high-exposure group males and females. No significant clinical findings were noted in any animals during the recovery period.

## - Body weight gain:

A transient reduction in mean body weight gain of high-exposed males during the first week of exposure.

## - Food consumption:

The high-exposure group males experienced slightly decreased food consumption means throughout the exposure period.

## - Haematology:

No adverse effects

## - Biochemistry:

No adverse effects

Let's mention however a statistically significant increases in blood urea nitrogen and aspartate-amino-transferase means in the high-exposure group males and females, respectively, at the study week 4 evaluation. Such increases were not considered to be of toxicological significance since blood urea nitrogen and aspartate-amino-transferase means in these groups were comparable to the control group after the two-week recovery period.

## - Urinalysis:

No adverse effects

## - Organ weights:

No significant changes were noted.

## - Gross pathology:

Gross findings in the animals that were found dead during the study (dark red content of ileum, dark red lungs, reddened and/or enlarged lymph nodes, etc.) were seen at a similar incidence in the control group or are not uncommon in rats.

## - Histopathology:

Test article-related microscopic findings were observed in the nasal turbinates of the high-exposure group rats that were found dead and in all treated groups at the study week 4 and 6 evaluations; however, the severity of some of the findings observed after the two-week recovery period suggested at least partial recovery from the irritative effects of the test article.

**Source** : ATOFINA, Paris-La Défense, France.

Atofina Paris La Défense Cedex

**Test condition** : TEST ORGANISMS:

- Source: Charles River Breeding Laboratories (Portage, Michigan)

- Age: 36 to 43 days

- Weight at study initiation: 235 ± 29.4 g for males, 188 ± 16.9 g for females

- Number of animals: 120 rats : 15 males + 15 females / dose group (3 dose groups + 1 control group)

### HOUSING

The animals were housed individually in suspended stainless steel cages

### FOOD and WATER

- Food: PMI certified rodent chow # 5002, ad libitum
- Water: filtered tap water, ad libitum

### ENVIRONMENTAL CONDITIONS

- Temperature : 71.2-73.0°F
- Relative humidity : 28.8-66%
- Light/dark cycle : 12h/12h
- Ventilation : no data

### ADMINISTRATION:

- Type of inhalation study: nose only
- Particle size:
  - . MMAD (Mass Median aerodynamic Diameter): 1.1
  - . Geometric Standard Deviation: 1.8
- Type or preparation of particles: Inspiron Model 002305-A nebulizer (Inertech Resources)
- Vehicle: filtered air
- Nominal / analytical concentrations:
  - 0.025 / 0.026 mg/l
  - 0.075 / 0.073 mg/l
  - 0.25 / 0.242 mg/l

SATELLITE GROUPS AND REASONS THEY WERE ADDED: none

### CLINICAL OBSERVATIONS AND FREQUENCY:

- Clinical signs: yes (twice a day on exposure days and once a day on non-exposure days)
- Mortality: yes (twice a day)
- Body weight: yes (one week prior initiation of test article exposure [day-7] and prior to necropsy).
- Food consumption: yes (one week before the beginning of exposure, then weekly)
- Ophthalmoscopic examination: no
- Haematology: yes  
Hemoglobin, hematocrit, red blood cell count, white blood cell count, differential leukocyte count, platelet count, mean cell volume, mean cell haemoglobin concentration, mean cell haemoglobin
- Biochemistry: yes
- Electrolytes: calcium, chloride, phosphorous, potassium, sodium,
- Enzymes: alkaline phosphatase, alanine-aminotransferase, aspartate-aminotransferase, gamma-glutamyl-transferase
- Other: albumin, blood creatinine, blood urea nitrogen, albumin/globulin, glucose, total bilirubin, total cholesterol, total serum protein, bile acids
- Urinalysis: yes  
urine volume, pH, specific gravity, proteins, glucose, ketones, bilirubin, nitrites, blood, urobilinogen, leukocytes, microscopy of sediments, appearance, color.

### ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):

- Weighted organs: adrenals, brain, heart, kidneys, liver, lungs, ovaries, spleen, testes with epididymides and thymus.
- Macroscopic examined

- Cardio-vascular and hematopoietic system: heart, aorta (thoracic), bone marrow, lymph node (bronchial, mesenteric, supratharyngeal), thymus, spleen
- Digestive system: tongue, salivary glands (maxillary), oesophagus, stomach, liver, gallbladder, pancreas, duodenum, jejunum, ileum, caecum, colon, rectum
- Glandular system: pituitary, thyroid, parathyroids, adrenal, mammary gland
- Nervous system: brain, spinal cord, sciatic nerve, eye (optic nerve)
- Respiratory system: nasal turbinates, trachea, lungs with bronchi
- Uro-genital system: kidney, bladder, ovary, uterus, vagina, testes, epididymides, seminal vesicle, prostate, Fallopian tubes
- Other: skin, muscle (vastus medialis)
- Microscopic: lungs and nasal cavity
- Cardio-vascular and hematopoietic system: heart, aorta (thoracic), bone marrow, lymph node (bronchial, mesenteric, supratharyngeal), thymus, spleen
- Digestive system: tongue, salivary glands (maxillary), oesophagus, stomach, liver, gallbladder, pancreas, duodenum, jejunum, ileum, caecum, colon, rectum
- Glandular system: pituitary, thyroid, parathyroids, adrenal, mammary gland
- Nervous system: brain, spinal cord, sciatic nerve, eye (optic nerve)
- Respiratory system: nasal turbinates, trachea, lungs with bronchi
- Uro-genital system: kidney, bladder, ovary, uterus, vagina, testes, epididymides, seminal vesicle, prostate, Fallopian tubes
- Other: skin, muscle (vastus medialis)

|                         |  |
|-------------------------|--|
| <b>Test substance</b>   | : OTHER EXAMINATIONS: none<br>: Test substance: Methanesulfonic acid<br>C AS no.: 75-75-2<br>Source: Elf Atochem NA<br>Batch number: M-12-E<br>Purity: the test substance was supplied as a 69.9% aqueous solution   |
| <b>Conclusion</b>       | : Exposure of albino rats to an aerosol of methane sulfonic acid resulted in changes in the clinical conditions of the animals at exposure levels of 0.073 and 0.242 mg/L, a transient reduced mean body weight gain in the 0.242 mg/L exposure level males, slightly reduced food consumption means in the 0.242 mg/L exposure level males and histopathologic lesions in the nasal turbinates of all exposed groups.<br>Based on the data obtained during the two-week recovery (nonexposure) period, the effects on the clinical conditions of the animals and body weight gains were completely reversible; histopathological lesions in the nasal turbinates were observed in all groups at the end of the recovery period. Based on the compound-induced lesions observed in the nasal turbinates, the no observed effect level (NOEL) for local irritation was considered to be less than 0.026 mg/L. The NOEL for systemic toxicity was considered to be 0.026 mg/L. |
| <b>Reliability Flag</b> | : (1) valid without restriction<br>: Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint   |

17.03.2006

(10)

|                             |   |   |
|-----------------------------|---|---|
| <b>Type</b>                 | : |   |
| <b>Species</b>              | : | rat   |
| <b>Sex</b>                  | : | male/female   |
| <b>Strain</b>               | : | Sprague-Dawley  |
| <b>Route of admin.</b>      | : | inhalation  |
| <b>Exposure period</b>      | : | 5 days  |
| <b>Frequency of treatm.</b> | : | 6 hours/day   |
| <b>Post exposure period</b> | : | no  |
| <b>Doses</b>                | : | 0.026, 0.082, 0.23 and 0.74 mg/L  |
| <b>Control group</b>        | : | yes, concurrent vehicle   |
| <b>NOAEL</b>                | : | = .082 mg/l   |
| <b>Method</b>               | : | other: EPA 40 CFR 792   |
| <b>Year</b>                 | : |   |
| <b>GLP</b>                  | : | yes   |
| <b>Test substance</b>       | : | other TS  |
| <b>Method</b>               | : | <p>- Analytical device:<br/>Ion chromatography, Intox Products particle size analyzer model 02-140/JB, Intox Products 25-mm filter and Mettler AE240 electronic balance (for gravimetric determination).</p> <p>- Statistical tests:<br/>One-way analysis of variance followed by a Dunnett's test using a Digital MicroVAX 3400 computer "with appropriate programming".</p>   |
| <b>Result</b>               | : | <p>- Mortality:<br/>Two and three test article-related deaths occurred in the 0.23 and 0.74 mg/L groups, respectively. All other animals survived to the scheduled necropsy.</p> <p>- Clinical signs:<br/>The predominant test article-related clinical sign in males and females in the 0.23 and 0.74 mg/L groups was rales.</p> <p>- Body weight gain:<br/>Mean body weight losses and/or reduced mean body weight gains were noted in males and females in the 0.74 mg/L group during days 0-1 through 2-3; a slight mean body weight loss occurred in males in this group during day 4-5. Mean body weights were generally reduced in males and females in this group throughout the study.</p> <p>- Food consumption:<br/>Food consumption was generally reduced throughout the study relative to the control group values in males and females in the 0.74 mg/L group.</p> <p>- Organ weights:<br/>Organ weights were unaffected by test article administration at any exposure level.</p> <p>- Gross pathology:<br/>No treatment-related macroscopic findings were noted in treated animals</p> <p>- Histopathology:<br/>Microscopic findings in the nasal cavities that were considered to be related to exposure to the test article included mucosal necrosis, suppurative inflammation and/or nasal exudate in males and females in the 0.23 and 0.74 mg/L groups.</p> |
| <b>Source</b>               | : | ATOFINA, Paris-La Défense, France.  |

|                       |   |
|-----------------------|---|
| <b>Test condition</b> | <p>Atofina Paris La Défense Cedex</p> <p>: TEST ORGANISMS:</p> <ul style="list-style-type: none"><li>- Source: Charles River Breeding Laboratories (Portage, Michigan)</li><li>- Age: 36 days</li><li>- Weight at study initiation: 214 ± 16 g for males, 159 ± 11.7 g for females</li><li>- Number of animals: 50 rats : 5 males + 5 females / dose group (4 dose groups + 1 control group)</li></ul> <p>HOUSING</p> <p>The animals were housed individually in suspended stainless steel cages</p> <p>FOOD and WATER</p> <ul style="list-style-type: none"><li>- Food: PMI certified rodent chow # 5002, ad libitum</li><li>- Water: filtered tap water, ad libitum</li></ul> <p>ENVIRONMENTAL CONDITIONS</p> <ul style="list-style-type: none"><li>- Temperature : 73-76°F</li><li>- Relative humidity : 30-36%</li><li>- Light/dark cycle : 12h/12h</li><li>- Ventilation : no data</li></ul> <p>ADMINISTRATION:</p> <ul style="list-style-type: none"><li>- Type of inhalation study: nose only</li><li>- Particle size: see corresponding attached document</li><li>- Type or preparation of particles: De Vilbis glass nebulizer</li><li>- Vehicle: air</li><li>- Nominal / analytical concentrations:<br/>0.022 / 0.0259 mg/l<br/>0.066 / 0.0818 mg/l<br/>0.22 / 0.2264 mg/l<br/>0.66 / 0.7387 mg/l</li></ul> <p>SATELLITE GROUPS AND REASONS THEY WERE ADDED: none</p> <p>CLINICAL OBSERVATIONS AND FREQUENCY:</p> <ul style="list-style-type: none"><li>- Clinical signs: yes (twice a day)</li><li>- Mortality: yes (twice a day)</li><li>- Body weight: yes (one week prior initiation of test article exposure [day-7], once before the allocation of animals to groups [day-1], every day of treatment and then on day 5, prior to necropsy).</li><li>- Food consumption: yes (daily, one week before the beginning of exposure)</li><li>- Ophthalmoscopic examination: no</li><li>- Haematology: no</li><li>- Biochemistry: no</li></ul> <p>ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):</p> <ul style="list-style-type: none"><li>- Macroscopic examined and weighted organs: external surface, all orifices, cranial, thoracic, abdominal and pelvic cavities including viscera, with particular attention paid to the nasal and lung tissues. At the time of necropsy, gross lesions, heads and lungs were collected and placed in a 10% neutral buffered formalin.</li><li>- Microscopic: lungs and nasal cavity</li></ul> <p>OTHER EXAMINATIONS: none</p> |
|-----------------------|---|

**Test substance** : Test substance: Methanesulfonic acid  
 C AS no.: 75-75-2  
 Source: Elf Atochem NA  
 Batch number: L-04-D  
 Purity: the test substance was supplied as a 69.9% aqueous solution

**Attached document** : 75-75-25 -day inhalation test - Particle size.bmp

| Analytical concentration (mg/L) | DM200 (µg/L) | AOSD |
|---------------------------------|--------------|------|
| 0.0266                          | 1.4          | 1.7  |
| 0.0816                          | 1.4          | 1.8  |
| 0.2564                          | 1.4          | 1.8  |

DM200: Mean Median Average Diameter  
 AOSD: Average Geometric Standard Deviation

**Conclusion** : Methane sulfonic acid, administered via nose-only inhalation for six hours per day for five consecutive days, caused mortalities, clinical signs of toxicity and microscopic effects on nasal cavities at exposure levels of 0.23 and 0.74 mg/L and inhibition of body weight gain and food consumption at an exposure level of 0.74 mg/L. No signs of systemic toxicity were observed at exposure levels of 0.026 and 0.082 mg/L. The NOEL for systemic toxicity was found to be 0.082 mg/L. Based on data obtained, exposure level of 0.025, 0.075 and 0.25 mg/L were chosen for a subsequent 28-day inhalation study.

**Reliability** : (1) valid without restriction  
 17.03.2006

(11)


**Type** :  
**Species** : rat  
**Sex** : male/female  
**Strain** : Wistar  
**Route of admin.** : oral feed  
**Exposure period** : 7 days  
**Frequency of treatm.** : ad libitum  
**Post exposure period** : none  
**Doses** : Males: 0, 51, 185, 420, 1805 mg/kg bw/d  
 Females: 0, 55, 201, 551, 2122 mg/kg bw/d  
**Control group** : yes, concurrent no treatment  
**NOAEL** : >= 1805 - 2122 mg/kg bw  
**Method** : other  
**Year** :  
**GLP** : no  
**Test substance** :

**Method** : Statistical tests:  
 For growth effects the means for each sex were calculated and compared after adjustment of the individual weights of each rat to a change in weight. over their weight on the morning of their first day of dosing. The results of weight changes were intercompared for the dosage groups by use of Bartlett's test for homogeneity of variance, by the analysis of variance and by Duncan's multiple range test. The latter was used, if F for the analysis of variance was significantly high, to delineate which groups differed from the other. If Bartlett's test indicated heterogeneous variances, the F-test was used for any paired-group comparison. If these individual F-tests were not significant, Student's t-test was used; if significant, the means were compared by the Cochran t-test. The fiducial

## 5. Toxicity

Id 75-75-2

Date 10.10.2006

- limit of 0.05 was employed as the critical level of difference not believed to be produced by chance.
- Result** : Mortality: no death occurred  
Body weight: no significant variation  
Organ weights: no relevant changes in terms of doses
- Source** : Detailed data are presented in the attached document.  
: ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex
- Test condition** : TEST ORGANISMS:  
- Source: Harlan Industries, Cumberland.  
- Age: 30 days  
- Weight at study initiation: 84 to 147 g (males) and 79 to 130 g (females)  
- Number of animals: 5 rats / dose
- ADMINISTRATION:  
- Vehicle: distilled water then mixed with food  
- Concentration in diet: 0.043%, 0.159%, 0.382% and 1.635% (for males) and 0.045%, 0.183%, 0.479% and 1.80% (for females)  
- Food consumption: 13.9 to 16.9 g of food/day  
- Other: After the first day of dose, the dosage level of the rats on 10 mg/kg of methane sulfonic acid in diets was increased to 2000 mg/kg/day for the remainder of the week.
- SATELLITE GROUPS AND REASONS THEY WERE ADDED: none
- CLINICAL OBSERVATIONS AND FREQUENCY:  
- Clinical signs: yes (at least once a day)  
- Mortality: yes (at least twice a day)  
- Body weight: yes (three times during the week)  
- Food consumption: yes (no data about frequency)  
- Water consumption: no data  
- Ophthalmoscopic examination: no  
- Haematology: no  
- Biochemistry: no  
- Urinalysis: no
- ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):  
- Macroscopic examined and weighted organs: liver and kidneys  
- Microscopic: none
- Test substance** : Test substances: Methane sulfonic acid  
CAS no.: 75-75-2  
Source: South Charleston, WV.  
Batch number: 38-119  
Purity: 98% (anhydrous grade)
- Attached document** : 75-75-2 Sub -acute EPA-OTS0536043.bmp
- 
- Conclusion** : None of the rats orally exposed to methane sulfonic acid (up to 1800 mg/kg/day) or to its potassium salt (2000 mg/kg/day) died during this 7-day study.  
Furthermore, none of the measured parameters (food

consumption, body weight change, liver and kidney weight) was affected by the exposure. Consequently, NOAEL can be valued at 1805 mg/kg/day for males and 2122 mg/kg/day for females.

**Reliability** : (2) valid with restrictions (43)  
17.03.2006

### 5.5 GENETIC TOXICITY 'IN VITRO'

**Type** : Salmonella typhimurium reverse mutation assay  
**System of testing** : Strains: TA1535, TA1537, TA1538, TA98 and TA100  
**Test concentration** : 100, 500, 1000, 2500 and 5000 µg/plate  
**Cycotoxic concentr.** : 5000 and 10000 µg/plate on TA98 and TA100  
**Metabolic activation** : with and without  
**Result** : negative  
**Method** : OECD Guide-line 471  
**Year** : 1983  
**GLP** : yes  
**Test substance** :

**Method** : Analytical device: Artek 980 electronic colony counter  
Statistical test: no data

**Result** : BACTERIAL TOXICITY  
Methane sulfonic acid induced a marked toxicity on two tester strains: TA98 and TA100 at 1000 µg/plate with and without metabolic activation. In addition it was observed that the S9 mix preparation precipitated at those two concentrations.  
Without metabolic activation at 5000 µg/plate, a moderate toxic effect was noted on TA100, whereas on TA98 a decrease of the revertant colonies number with a sparse background was noted.  
Therefore, the following concentrations were selected for the genotoxicity study: 100, 500, 1000, 2500 and 5000 µg/plate.

**GENOTOXIC EFFECTS:**  
Whatever conditions used (metabolic activation or not), methanesulfonic acid did not induce any increase of revertant colonies per plate, at any dosages. This is true for both assays.

**PRECIPITATION:**  
A precipitation of the S9 mix preparation was observed from the concentration of 2500 µg/plate, in a concentration-related effect of increasing intensity in the first assay, while it only appeared at 5000 µg/plate in the second one.

**Source** : TEST-SPECIFIC CONFOUNDING FACTORS: none  
: ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex

**Test condition** : EXPERIMENTAL CONDITIONS:  
- Number of replicates: 3/dose  
- Metabolic activation: S9-mix (from male Sprague-Dawley rats, treated by Aroclor 1254)  
- Vehicle: distilled water  
- Negative control: distilled water  
- Positive controls:  
. for TA1535 and TA100: sodium azide (5µg/plate)

|                             |  |      |
|-----------------------------|--|------|
|                             | <ul style="list-style-type: none"> <li>. for TA1538 and TA98: 2-nitrofluorene (5µg/plate)</li> <li>. for TA1537: 9 -aminoacridine (100µg/plate)</li> <li>. for all strains: 2-aminoanthracene (5µg/plate except 2.5µg/plate for TA1537)</li> <li>- Pre-incubation time: 20 minutes</li> <li>- Pre-incubation temperature: 37°C</li> <li>- Incubation time: 48 hours</li> <li>- Incubation temperature: 37°C</li> </ul>   |      |
|                             | <p>EXAMINATION:</p> <ul style="list-style-type: none"> <li>- Bacterial toxicity (performed on TA100 and TA98 at 500, 1000, 5000 and 10000 µg/plate)</li> <li>- Number of revertants / plate</li> </ul>   |      |
|                             | <p>CRITERIA FOR EVALUATING RESULTS:</p> <ul style="list-style-type: none"> <li>- Positivity criteria for cytotoxicity: <ul style="list-style-type: none"> <li>. reduced numbers of revertant colonies/plate compared with control plates</li> <li>. sparsity of bacterial background lawn when compared with control plates</li> </ul> </li> <li>- Positivity criteria: <ul style="list-style-type: none"> <li>. number of revertants at least twice that of spontaneous revertants</li> <li>. dose-related pattern</li> <li>. number of revertant/nmol &gt; 0.01</li> <li>. reproducibility of the positive response</li> </ul> </li> </ul> |      |
| <b>Test substance</b>       | : Test substance: Methanesulfonic acid<br>CAS no.: 75-75-2<br>Source: Pennwalt<br>Purity: 98.8%  |      |
| <b>Conclusion</b>           | : No genotoxicity was observed on tested strains (TA1535, TA1537, TA1538, TA98 and TA100) up to the cytotoxicity threshold (5000 µg/plate).  |      |
| <b>Reliability</b>          | : (1) valid without restriction  |      |
| <b>Flag</b><br>17.03.2006   | : Material Safety Dataset, Critical study for SIDS endpoint  | (42) |
| <b>Type</b>                 | : Salmonella typhimurium reverse mutation assay  |      |
| <b>System of testing</b>    | : Strains: TA98, TA100, TA1535, TA1537, TA1538   |      |
| <b>Test concentration</b>   | : 10, 32, 100, 316, 1000 µg/plate  |      |
| <b>Cycotoxic concentr.</b>  | : 1000 µg/plate  |      |
| <b>Metabolic activation</b> | : with and without   |      |
| <b>Result</b>               | : negative   |      |
| <b>Method</b>               | : OECD Guide-line 471  |      |
| <b>Year</b>                 | : 1983   |      |
| <b>GLP</b>                  | : yes  |      |
| <b>Test substance</b>       | :  |      |
| <b>Result</b>               | : No increases in reversion to prototrophy were obtained with any of the five bacterial strains at the compound level tested, either in the presence or absence of S9 mix.   |      |
|                             | Inhibition of growth, observed as thinning of the background lawn of non revertants cells and reduction in colony numbers, occurred in all strains following exposure to 1000 µg/plate.  |      |
| <b>Source</b>               | : ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex   |      |
| <b>Test condition</b>       | : EXPERIMENTAL CONDITIONS: <ul style="list-style-type: none"> <li>- Number of replicates: 3 plates per dose, 2 independant studies</li> <li>- Metabolic activation: S9-mix</li> </ul>  |      |

|                             |  |      |
|-----------------------------|--|------|
|                             | <ul style="list-style-type: none"> <li>- Vehicle: distilled water</li> <li>- Negative control: distilled water</li> <li>- Positive controls: sodium azide, 2-nitrofluorene, 9-aminoacridine, 2-aminoanthracene and benzo(a)pyrene</li> <li>- Pre-incubation time: none (direct plate incorporation)</li> <li>- Pre-incubation temperature: not relevant</li> <li>- Incubation time: 48 hours</li> <li>- Incubation temperature: 37°C</li> </ul>                                      |      |
|                             | EXAMINATION:   |      |
|                             | <ul style="list-style-type: none"> <li>- Growth inhibition</li> <li>- Number of revertants / plate</li> </ul>  |      |
|                             | CRITERIA FOR EVALUATING RESULTS:   |      |
|                             | no data  |      |
| <b>Test substance</b>       | : Test substance: Methanesulfonic acid<br>CAS no.: 75-75-2<br>Source: Pennwalt<br>Batch number: K15J<br>Purity: 70% in water   |      |
| <b>Conclusion</b>           | : Methane sulfonic acid is devoid of mutagenic activity.   |      |
| <b>Reliability</b>          | : (1) valid without restriction  |      |
| <b>Flag</b>                 | : Material Safety Dataset, Critical study for SIDS endpoint  |      |
| 17.03.2006                  |  | (35) |
| <b>Type</b>                 | : Salmonella typhimurium reverse mutation assay  |      |
| <b>System of testing</b>    | : Strains: TA100, TA1535   |      |
| <b>Test concentration</b>   | : 384.4 to 12300 µg/plate  |      |
| <b>Cycotoxic concentr.</b>  | : no data  |      |
| <b>Metabolic activation</b> | : with and without   |      |
| <b>Result</b>               | : negative   |      |
| <b>Method</b>               | : other: Mutation Res., 113: 173-215, 1983   |      |
| <b>Year</b>                 | : 1989   |      |
| <b>GLP</b>                  | : no   |      |
| <b>Test substance</b>       | :  |      |
| <b>Result</b>               | : see attached document  |      |
| <b>Source</b>               | : ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex   |      |
| <b>Test condition</b>       | : EXPERIMENTAL CONDITIONS: <ul style="list-style-type: none"> <li>- Number of replicates: 3/dose</li> <li>- Metabolic activation: S9-mix (from male Sprague-Dawley rats, treated by Aroclor 1254)</li> <li>- Vehicle: distilled water</li> <li>- Negative control: distilled water</li> <li>- Positive control: benzo(a)pyrene (S9+) and diepoxybutane (S9-)</li> <li>- Pre-incubation: no</li> <li>- Incubation time: no data</li> <li>- Incubation temperature: no data</li> </ul> |      |
|                             | EXAMINATION :  |      |
|                             | <ul style="list-style-type: none"> <li>- Bacterial toxicity</li> <li>- Number of revertants / plate. The test was repeated.</li> </ul>   |      |
| <b>Test substance</b>       | : Test substance: Methanesulfonic acid<br>CAS no.: 75-75-2<br>Source: Aldrich<br>Batch number: no data<br>Purity: 99%  |      |
| <b>Attached document</b>    | : 75-75-2 Ames test (Zeiger).bmp   |      |



|                             |   |   |      |
|-----------------------------|---|---|------|
| <b>Reliability</b>          | : | (2) valid with restrictions<br>Only 2 strains tested and scarce data.   |      |
| 17.03.2006                  |   |   | (44) |
| <b>Type</b>                 | : | other: Ames-derived gradient technique  |      |
| <b>System of testing</b>    | : | E. coli (WP2 and WP2 uvrA-), S. typhimurium (G46, TA1535, TA100, C3076, TA1537, D3052, TA1538, TA98)  |      |
| <b>Test concentration</b>   | : | No data available   |      |
| <b>Cycotoxic concentr.</b>  | : |   |      |
| <b>Metabolic activation</b> | : | with and without  |      |
| <b>Result</b>               | : | negative  |      |
| <b>Method</b>               | : | other   |      |
| <b>Year</b>                 | : | 1979  |      |
| <b>GLP</b>                  | : | no  |      |
| <b>Test substance</b>       | : |   |      |
| <b>Result</b>               | : | No significant colonies appeared all along the streaks.   |      |
| <b>Source</b>               | : | ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex  |      |
| <b>Test condition</b>       | : | <p>PRINCIPLE OF THE TEST:</p> <p>It is a reverse mutation test (like the Ames test). Two agar layers are poured in a Petri dish. Only the upper layer contains the test substance. The plate is incubated for 2 hours at room temperature in order to let the test substance diffuse in the lower layer, creating thus a gradient of concentrations.</p> <p>A streaking device, made of 10 sterile micropipets is used to seed the plate. Pipets are dipped in bacterial suspension and drawn down across the plate.</p> <p>Colonies growing in deep agar are assumed to have been exposed to lower concentration than those growing on the surface.</p> <p>EXPERIMENTAL CONDITIONS:</p> <ul style="list-style-type: none"> <li>- Number of replicates: 3/dose</li> <li>- Metabolic activation: S9-mix (from male Fischer rats, treated by Aroclor 1254)</li> <li>- Vehicle: distilled water</li> <li>- Negative control: no compound</li> <li>- Positive controls: streptozotocin (S9-) and acetylaminofluorene (S9+)</li> <li>- Incubation time: 48 hours</li> <li>- Incubation temperature: 37°C</li> </ul> <p>EXAMINATION:</p> <p>Number of colonies all along the streaks.</p> <p>CRITERIA FOR EVALUATING RESULTS:</p> <p>Negative result: a very pale streak of bacterial growth is seen along the inoculation streak.</p> <p>Positive result: discrete colonies appear in a pale background lawn with and increased density along the increasing gradient.</p> |      |
| <b>Test substance</b>       | : | Test substance: Methanesulfonic acid  |      |

## 5. Toxicity

Id 75-75-2  
Date 10.10.2006

|                             |   |      |
|-----------------------------|---|------|
|                             | CAS no.: 75-75-2<br>Source: no data<br>Batch number: no data<br>Purity: no data   |      |
| <b>Reliability</b>          | : (3) invalid<br>Concentrations are not checked all along the gradient.<br>No preliminary study focused on compound diffusion in agar is available.<br>Tested concentrations are guessed rather than known.   |      |
| 17.03.2006                  |   | (29) |
| <b>Type</b>                 | : DNA damage and repair assay   |      |
| <b>System of testing</b>    | : Escherichia coli P3478E   |      |
| <b>Test concentration</b>   | : 25 µl/plate (37 µg/plate)   |      |
| <b>Cycotoxic concentr.</b>  | :   |      |
| <b>Metabolic activation</b> | : without   |      |
| <b>Result</b>               | : negative  |      |
| <b>Method</b>               | : other   |      |
| <b>Year</b>                 | : 1976  |      |
| <b>GLP</b>                  | : no  |      |
| <b>Test substance</b>       | :   |      |
| <b>Result</b>               | : Diameters of growth inhibition zone for deficient and wild strains were respectively 33 and 30 mm.<br>Differential is 3 mm and therefore no significant.<br>Consequently, methane sulfonic acid is not mutagenic.   |      |
| <b>Source</b>               | : ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex  |      |
| <b>Test condition</b>       | : PRINCIPLE:<br>Escherichia coli, which are deficient in DNA polymerase and therefore repair-deficient are exposed to test substance.<br>Wild bacteria are simultaneously exposed to the same substance.<br>Mutagenic effect is measured by the difference of diameters of inhibition growth zone between DNA polymerase deficient and wild strains.<br><br>EXPERIMENTAL CONDITIONS:<br>- Number of replicates: 2<br>- Vehicle: none<br>- Negative control: no<br>- Positive control: dimethyl sulfate, ampicillin and colistin<br>- Incubation time: 16 hours<br>- Incubation temperature: 37°C<br><br>EXAMINATION:<br>Zone diameters of DNA polymerase deficient and that of wild strains were measured in millimeters.<br>Difference was calculated.<br><br>CRITERIA FOR EVALUATING RESULTS:<br>A differential greater than 4 mm was considered as positive. |      |
| <b>Test substance</b>       | : Test substance: Methanesulfonic acid<br>CAS no.: 75-75-2<br>Source: no data<br>Batch number: no data<br>Purity: no data   |      |
| <b>Reliability</b>          | : (3) invalid<br>The authors are themselves unforthcoming about the ability of this test to detect real mutagens.   |      |
| 17.03.2006                  |   | (25) |

## 5.6 GENETIC TOXICITY 'IN VIVO'

**Type** : Micronucleus assay  
**Species** : mouse  
**Sex** : male/female  
**Strain** : CD-1  
**Route of admin.** : gavage  
**Exposure period** : single administration, sacrifice at 24h, 48h or 72h  
**Doses** : 0, 20, 100, 500 mg/kg  
**Result** : negative  
**Method** : other: not specified, comparable to OECD Guide-line 474  
**Year** :  
**GLP** : yes  
**Test substance** :

**Method** : A preliminary toxicity test was first conducted, using dosages of 125, 250, 500, 1000 and 2500 mg/kg. Subsequently, male and female mice were given a single dose of methanesulphonic acid at 20, 100 or 500 mg/kg. In all cases methanesulphonic acid was dosed orally, in distilled water. Concurrent vehicle and positive control groups of mice were similarly dosed with distilled water or chlorambucil (30 mg/kg) respectively.

Five males and five females from each group were killed 24 hours after treatment; further lots of five males and five females, given methanesulphonic acid at 20, 100 or 500 mg/kg or the vehicle control, were killed 48 and 72 hours after treatment.

Bone marrow smears on glass slide were made from each animal. These slides were then stained and prepared for examination.

A total of at least 2000 erythrocytes per animal was then examined for the presence of micronuclei, using the light microscope. Calculated values of micronuclei per 1000 polychromatic erythrocytes were analysed statistically using the Mann-Whitney U test. The ratio of polychromatic/mature cells was also calculated for each animal, as an indicator of medullar toxicity.

**Result** : RANGE-FINDING STUDY

- 2500 mg/kg: one female died approximately 30 seconds post-dose. One male was killed in extremis approximately 30 minutes post-dose and the remaining male and female were killed in extremis 2.5 hours post-dose; signs included hunched posture, piloerection, slow laboured breathing and inability to move.

- 1000 mg/kg: one male was found dead in its cage approximately 21 hours post-dose and the remaining male and both females were killed in extremis approximately 21 hours post-dose; signs included hunched posture, lethargy, piloerection, slow laboured breathing and inability to move.

- All other animals dosed with methanesulphonic acid survived to scheduled termination. Piloerection was noted in all animals in the 24 hour period following dosing at 500 mg/kg. No adverse reactions to treatment were recorded for any other group of animals dosed with methanesulphonic acid.

Incidences of weight loss were noted but these were small and not dose-related.  
There was some evidence of toxicity of methanesulphonic acid (as evidenced by depression in bone marrow proliferation) to the bone marrow of mice treated at 250 or 500 mg/kg.

**MAIN STUDY****- MORTALITY:**

Two male animals dosed with 500 mg/kg were found dead in their cage approximately 21 hours post-dose.  
One animal exhibiting pilo-erection, severe rales and loss of facial hair was killed approximately 48h after treatment.  
Results from those three animals have been excluded from the analysis

**- CLINICAL SIGNS:**

All surviving male mice of the 500 mg/kg group showed pilo-erection. One of them exhibited rales. One female presented such rales too.  
All other animals remained asymptomatic.

**- NUMBER OF MICRONUCLEATED ERYTHROCYTES PER ANIMALS:**

No significant variation in treated animals was reported, whatever the dose after 24, 48h and 72h.  
However, chlorambucil group exhibited a significant increase of micronucleated polychromatic erythrocytes.

**- PROPORTION OF IMMATURE ERYTHROCYTES AMONG TOTAL ERYTHROCYTES (PCE/NCE RATIO):**

No real indication of bone marrow toxicity, as evidenced by depression bone marrow proliferation was noted in any group treated by methane sulfonic acid.

**Source**

: ATOFINA, Paris-La Défense, France.

Atofina Paris La Défense Cedex

**Test condition**

: TEST ORGANISMS:

- Source: Charles River Breeding Laboratories, UK
- Age: 4-5 weeks
- Body weight at study initiation: 18.3 -27.5 g
- Number of animals per dose: 5 males + 5 females
- Acclimatization period: at least 4 days

**HOUSING**

The animals were housed in single-sex groups of 2 or 5 in high density polypropylene cages with stainless steel tops.

**FOOD and WATER**

- Food: LAD1 (Labsure , UK), ad libitum
- Water: tap water, ad libitum

**ENVIRONMENTAL CONDITIONS**

- Temperature : 21 +/- 2°C
- Relative humidity : 55 +/- 15 %
- Light/dark cycle : 12h/12h
- Ventilation : 15 cycles/hour

**ADMINISTRATION:**

- Vehicle: distilled water
- Administration volume: 10 ml/kg
- Frequency of treatment: single administration
- Positive control: chlorambucil (30 mg/kg)

|                         |   |
|-------------------------|---|
|                         | - Negative control: distilledwater  |
|                         | EXAMINATIONS:   |
|                         | - Clinical observations: daily  |
|                         | - Mortality: daily  |
|                         | - Body weight: on day of treatment and again immediately before termination   |
|                         | - Tissue examined: bone marrow  |
|                         | - Slide preparation: according to the standard procedure  |
|                         | - Number of cells analyzed per animal: at least 2000 erythrocytes   |
|                         | - Equipment: light microscope   |
|                         | - Statistical test: Mann-Whitney U-test   |
| <b>Test substance</b>   | : Test substance: Methanesulfonic acid<br>CAS no.: 75-75-2<br>Source: no data<br>Batch number: no data<br>Purity: 70% in water  |
| <b>Conclusion</b>       | : There was no evidence of induced chromosomal or other damage leading to micronucleus formation in polychromatic erythrocytes of treated mice 24, 48 or 72 hours after oral administration of methanesulphonic acid. |
| <b>Reliability Flag</b> | : (1) valid without restriction<br>: Material Safety Dataset, Critical study for SIDS endpoint  |
| 17.03.2006              | (36)  |

## 5.7 CARCINOGENICITY

### 5.8.1 TOXICITY TO FERTILITY

|                                  |  |
|----------------------------------|--|
| <b>Type</b>                      | : other: reproduction/developmental toxicity screening test  |
| <b>Species</b>                   | : rat  |
| <b>Sex</b>                       | : male/female  |
| <b>Strain</b>                    | : Sprague-Dawley   |
| <b>Route of admin.</b>           | : gavage   |
| <b>Exposure period</b>           | : * in males: during 4w before mating, the mating period (2w) and until sacrifice.<br>* in females: during 4w before mating, the mating period (2w), pregnancy (3w), lactation until day 4 pp inclusive, and until sacrifice (D5 pp) |
| <b>Frequency of treatm.</b>      | : 7 days per week  |
| <b>Premating exposure period</b> |  |
| <b>Male</b>                      | : 4 weeks  |
| <b>Female</b>                    | : 4 weeks  |
| <b>Duration of test</b>          | :  |
| <b>No. of generation studies</b> | : 1  |
| <b>Doses</b>                     | : 250, 500 and 1000 mg/kg/d  |
| <b>Control group</b>             | : yes, concurrent vehicle  |
| <b>NOAEL parental</b>            | : 1000 mg/kg bw  |
| <b>NOAEL F1 offspring</b>        | : 1000 mg/kg bw  |
| <b>Method</b>                    | : OECD Guide-line 421  |
| <b>Year</b>                      | : 1995   |
| <b>GLP</b>                       | : yes  |
| <b>Test substance</b>            | :  |
| <b>Method</b>                    | : CLINICAL EXAMINATIONS<br>- Morbidity and mortality: at least twice a day<br>- Clinical signs: at least once a day  |

- Body weight:
  - . males: on day 1, then once a week until sacrifice
  - . females: on day 1, then once a week until mated, then on days 0, 7, 14 and 20 pc and on days 1 and 4 pp.
- Food consumption
  - . males: once a week (except during the mating period) until sacrifice
  - . females: once a week during the pre-mating period and then on the following intervals: days 0-7, 7-14, 14-20 post-coitum, and days 1-4 post-partum.

### MATING

- Mating procedure: one female was placed with one male from the same dose-level group

### PARTURITION

Females were allowed to drop their litters normally and rear their progeny until day 4 post partum

### OBSERVATIONS OF THE PROGENY DURING THE POSTPARTUM PERIOD

- Litter size: total litter size and numbers of pups of each sex were recorded as soon as possible after birth. The litters were observed daily.
- Clinical signs: daily
- Body weight: days 1 and 4 pp

### PATHOLOGY

- Sacrifice
  - . males: after the end of the mating period,
  - . females: on day 5 postpartum,
  - . females which had not delivered on day 25 post-coitum: from day 25 post-coitum,
  - . females which did not mate: at least 1 week after the end of the mating period,
  - . pups: on day 5 postpartum.
- Organ weights: testes and epididymides
- Macroscopic post-mortem examination: on all parent animals. In all females, the number of implantation sites and corpora lutea were recorded.
- Pups: gross external examination before sacrifice
- Preservation of tissues: ovaries, prostate, seminal vesicles, uterus (horns and cervix), vagina, in 10% buffered formalin. Testes and epididymides, in Bouin's fluid
- Microscopic examination: ovaries, testes and epididymides (with special emphasis on stages of spermatogenesis and histopathology of interstitial testicular cell structure) of all males and females in the control and high-dose groups.

### Result

#### : CHEMICAL ANALYSES OF THE DOSAGE FORMS

- Stability: satisfactory stability of the 25 and 100 mg/mL solutions over a 9-day period at +4°C
- Concentration: satisfactory agreement ( $\pm 10\%$ ) between the nominal and actual concentrations

### CLINICAL EXAMINATIONS

- Mortality
  - . Males: no deaths in the control group or in the 250 or 500 mg/kg/day groups.
  - At 1000 mg/kg/day, one male on day 33. No major factor contributing to death was established.
  - . Females: no deaths in any group during the pre-mating period.

One female given 250 mg/kg/day was found dead on day 10 post-coitum. This death was consequently considered to be accidental and not related to the treatment.

- Clinical symptoms

. Males: no clinical signs at 250 and 500 mg/kg/day. At 1000 mg/kg/day, ptyalism was transiently observed in 4/11 males from days 20 or 21 of dosing.

. Females: no clinical signs at 500 mg/kg/day during the pre-mating and pregnancy periods. At 250 mg/kg/day, regurgitation was observed during the pre-mating period in two females from days 22 to 24 or days 26 to 27, and in three other females for 1 or 3 consecutive days of the pregnancy period. This sign was not dose-related and was therefore considered to be caused by difficult gavage. At 1000 mg/kg/day, ptyalism was observed in 3/12 females on day 20 of the pre-mating period.

The ptyalism (excess of salivation), noted in four males and three females given 1000 mg/kg/day, is commonly noted following gavage and is not considered as an adverse effect. There were no clinical signs at any dose-level during the lactation period.

- Body weight

. Males: no effect related to treatment

. Females: no effect related to treatment

- Food consumption: no treatment-related effect in males and females

MATING AND FERTILITY DATA

- Mating index: no treatment-related effect

- Pre-coital interval: no treatment-related effect

- Fertility index: no treatment-related effect

- Duration of gestation : no treatment-related effect

- Delivery data: no treatment-related effect

- Post-natal and neo-natal losses: no treatment-related effect

OBSERVATION OF THE PUPS AT BIRTH

- Mean number of liveborn pups per litter: no treatment-related effect

Macroscopic observation: no treatment-related effect

OBSERVATION OF THE PUPS AFTER BIRTH

- Mortality: no treatment-related effect

- Clinical signs: no treatment-related effect

- Pup body weight: no treatment-related effect

- Sex ratio: no treatment-related effect

PATHOLOGY

- Organ weights :(Table 22, Appendix 28)

Minor differences, considered to be of no toxicological significance, were observed in the weights of testes and epididymides between treated and control males.

- Macroscopic post-mortem examination : no treatment-related effect

- Microscopic examination:

. Testicular Staging: No treatment-related changes were observed.

. Ovaries: No treatment-related changes were observed.

Semi-quantitative evaluation of the morphological characteristics of ovarian physiology:

|                        |   |      |
|------------------------|---|------|
| Dose-level (mg/kg/day) | 0 | 1000 |
|------------------------|---|------|

|                                  |      |      |
|----------------------------------|------|------|
| Evaluation of ovarian follicles  |      |      |
| Very few                         | 3/12 | 5/12 |
| Few                              | 6/12 | 6/12 |
| moderate                         | 3/12 | 1/12 |
| Evaluation of corpora lutea      |      |      |
| Few                              | 7/12 | 6/12 |
| moderate                         | 5/12 | 4/12 |
| marked                           | 0/12 | 2/12 |
| Evaluation of follicular atresia |      |      |
| Very few                         | 2/12 | 4/12 |
| Few                              | 6/12 | 8/12 |
| moderate                         | 4/12 | 0/12 |

As no major difference was observed between the treated and control groups, it was concluded that there was no effect of treatment by the test item on the ovarian functions.

**Source** : ARKEMA, Paris-la-Défense, France (JFR)  
Atofina Paris La Défense Cedex

**Test condition** : ANIMALS  
- Number: 12 males and 12 females per dose  
- Strain : Sprague-Dawley CrI CD (SD) IGS BR  
- Breeder: Charles River Laboratories France, L'Arbresle, France  
- Age at the beginning of the treatment period: 10 weeks old

- Weight at the beginning of the treatment period: 408 g (range: 350 g to 441 g) for the males and 241 g (range: 211 g to 267 g) for the females  
- Acclimation: 11-days before the beginning of the treatment period

#### ENVIRONMENTAL CONDITIONS

- Temperature :  $22 \pm 2^{\circ}\text{C}$   
- Relative humidity :  $50 \pm 20\%$   
- Light/dark cycle : 12h/12h (7:00 - 19:00)  
- Ventilation : about 12 cycles/hour of filtered, non-recycled air.

#### HOUSING

The animals were housed individually in polycarbonate cages or in suspended wire-wash cages. Autoclaved wood shavings were provided as nesting material, a few days before delivery and during the lactation period

#### FOOD and WATER

- Food: A04 C pelleted maintenance diet ad libitum  
- Water: filtered (0.22  $\mu\text{m}$  filter) tap water ad libitum

#### TREATMENT

- Vehicle: purified water, obtained by reverse osmosis  
- Dosage form preparation: solution in the vehicle at 25, 50 and 100 mg/mL, expressed as active substance. The dosage forms were adjusted to a pH of 7.0 with NaOH  
- Volume: 10 ml/kg  
- Chemical analysis of the dosage forms:  
  . Stability: Two dosage forms (25 and 100 mg/mL) were sampled after 0, 4 and 9 days storage at  $+4^{\circ}\text{C}$   
  . Concentration: On weeks 1, 4 and 8

**Test substance** : Test article name: Methanesulfonic acid  
CAS no. : 75-75-2  
Source: ARKEMA  
Batch no. : 4810A

|                         |   |
|-------------------------|---|
| <b>Conclusion</b>       | : Purity: 70.50% in water<br>: The oral administration of METHANESULFONIC ACID at 250, 500 or 1000 mg/kg/day to male and female Sprague Dawley rats, was well tolerated at all dose-levels. There were no substance-induced effects on the male and female reproductive performance, nor on the progeny of the parental rats up to 1000 mg/kg/day. The no observed effect level (NOEL) for parental toxicity and for toxic effect on reproductive performance and on progeny is 1000 mg/kg/day. |
| <b>Reliability Flag</b> | : (1) valid without restriction<br>: Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint  |
| 02.01.2006              | (2)   |

### 5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

|                             |   |
|-----------------------------|---|
| <b>Species</b>              | : rat   |
| <b>Sex</b>                  | : female  |
| <b>Strain</b>               | : Sprague-Dawley  |
| <b>Route of admin.</b>      | : gavage  |
| <b>Exposure period</b>      | : from gestation day 6 through 15   |
| <b>Frequency of treatm.</b> | : once a day  |
| <b>Duration of test</b>     | : up to gestation day 20  |
| <b>Doses</b>                | : 25, 100 and 400 mg/kg   |
| <b>Control group</b>        | : yes, concurrent vehicle   |
| <b>NOAEL maternal tox.</b>  | : > 400 mg/kg bw  |
| <b>NOAEL teratogen.</b>     | : > 400 mg/kg bw  |
| <b>Result</b>               | : No developmental toxicity   |
| <b>Method</b>               | : OECD Guide-line 414 "Teratogenicity"  |
| <b>Year</b>                 | : 1981  |
| <b>GLP</b>                  | : yes   |
| <b>Test substance</b>       | : other TS  |
| <b>Result</b>               | : - Clinical observations:<br>No clinical signs that could be attributed to the test article were observed in the treated groups.<br><br>- Mortality:<br>No mortality until day 20 (necropsy)<br><br>- Body weight:<br>Body weight data in the treated groups were not affected by treatment.<br><br>- Food consumption:<br>Food consumption in the treated groups were not affected by treatment.<br><br>- Necropsy findings:<br>Intrauterine growth and survival were unaffected by test article administration at all dose levels.<br>The foetal malformations observed in the treated groups were considered to be spontaneous in origin.<br>The developmental variations observed in the treated groups occurred similarly in the control group and/or in a manner which was not dose-related. |
| <b>Source</b>               | : ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex  |
| <b>Test condition</b>       | : TEST ORGANISMS:<br>- Source: Charles River Breeding Laboratories (Portage,  |

Michigan)

- Age: approximately 70 days old
- Weight at study initiation: 266 ± 9.5 g
- Number of animals: 100 (25 females/dose group)

**ADMINISTRATION:**

- Vehicle: deionized water
- Concentration in vehicle: 25 or 50 mg/ml
- Total volume administered: 1, 4 or 8 ml/kg

**MATING PROCEDURES:**

The animals were paired for mating in the home cage of the male.

Positive mating criteria is not indicated.

**MATERNAL PARAMETERS ASSESSED:**

- Clinical observations: yes (twice a day, from day 0 through day 20)
- Mortality: yes (twice a day, from day 0 through day 20)
- Body weight: yes (daily on day 0, day 6 to day 16 and day 20)
- Food consumption: yes (daily on day 0, day 6 to day 16 and day 20)

**ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):**

All animals were euthanized on gestation day 20 for a scheduled laparohysterectomy. The uteri and ovaries were examined and the numbers of fetuses, early and late resorptions, total implantations and corpora lutea were recorded. Mean gravid uterine weights and net body weight changes were calculated for each group. The fetuses were weighed, sexed and examined for external, visceral and skeletal malformations and developmental variations.

**OTHER EXAMINATIONS:** none

- Test substance** : Test article name: Methanesulfonic acid  
C AS no. : 75-75-2  
Source: Elf Atochem  
Purity: 70.15% in water
- Conclusion** : Based on the results of this study, a dose level of 400 mg/kg/day was considered to be the no observable adverse effect level (NOAEL) for maternal toxicity and developmental toxicity of Methane Sulfonic Acid.
- Reliability Flag** : (1) valid without restriction  
: Material Safety Dataset, Directive 67/548/EEC, Critical study for SIDS endpoint

17.03.2006

(12)

- Species** : rat
- Sex** : female
- Strain** : Sprague-Dawley
- Route of admin.** : gavage
- Exposure period** : from gestation day 5 through 15
- Frequency of treatm.** : daily
- Duration of test** : sacrifice on GD20
- Doses** : 25, 50, 100, 200 and 300 mg/kg/d
- Control group** : yes, concurrent vehicle
- NOAEL maternal tox.** : 50 mg/kg bw
- NOAEL teratogen.** : > 300 ml/kg bw
- Result** : This range-finding study allows to perform a subsequent developmental toxicity study.

|                       |   |   |
|-----------------------|---|---|
| <b>Method</b>         | : | other: range finding study according to OECD Guide-line 414   |
| <b>Year</b>           | : |   |
| <b>GLP</b>            | : | yes   |
| <b>Test substance</b> | : | other TS  |
| <b>Result</b>         | : | <p>- Clinical observations:<br/>Treatment-related clinical signs observed consisted of rales, labored respiration and gasping in the 100, 200 and 300 mg/kg/d groups. Findings of red material around the nose and/or mouth in the 100, 200 and 300 mg/kg/d groups often correlated with occurrences of the aforementioned respiratory abnormalities. These findings appeared to be a function of the dosage concentration; rather the dosage level, as they were observed with similar frequency in the 100, 200 and 300 mg/kg/d groups, each of which received the test article at a concentration of 50 mg/ml.</p> <p>- Mortality:<br/>No mortality until day 20 (necropsy)</p> <p>- Body weight:<br/>slight mean body weight losses and reduction in food consumption occurred in the 100, 200 and 300 mg/kg/day groups during gestation days 6-9 when evaluated on a group mean basis. However, several animals in these groups experienced large, transient body weight losses and corresponding large decreases in food consumption on one or more occasions during the first days of the dosing period.<br/>Mean body weights, gravid uterine weights, net body weights and net body weight gains were unaffected by treatment at all dose levels.</p> <p>- Food consumption:<br/>Food consumption was slightly reduced in the 100, 200 and 300 mg/kg/d groups during gestation 6-9 when the group means were compared with the control group mean. This reduced food consumption seems to be the result of a localized gastro-intestinal effect due to the dosage concentration to these groups (50 mg/ml).</p> <p>- Necropsy finding:<br/>No treatment related internal necropsy findings were observed at any dose level.<br/>No effects were observed at any dose level on intrauterine growth and survival. No external developmental variations of malformations were observed in any of the fetuses in the treated groups.</p> |
| <b>Source</b>         | : | ATOFINA, Paris-La Défense, France.<br>Atofina Paris La Défense Cedex  |
| <b>Test condition</b> | : | <p>TEST ORGANISMS:</p> <ul style="list-style-type: none"> <li>- Source: Charles River Breeding Laboratories (Portage, Michigan)</li> <li>- Age: approximately 70 days old</li> <li>- Weight at study initiation: 261 +/- 10.7g</li> <li>- Number of animals: 48 (8 females/dose)</li> </ul> <p>ADMINISTRATION:</p> <ul style="list-style-type: none"> <li>- Vehicle: deionized water</li> <li>- Concentration in vehicle: 25 or 50 mg/ml</li> <li>- Total volume applied: 1, 2, 4 or 6 ml/kg</li> </ul> <p>MATING PROCEDURES:</p>   |

The animals were paired for mating in the home cage of the male.  
Positive mating criteria in not specified.

## PARAMETERS ASSESSED DURING STUDY:

- Body weight gain: on day 0, 6 to 16 and on day 20
- Food consumption: on day 0, 6 to 16 and on day 20
- Clinical observations:
- Mortality: twice a day, from day 0 through day 20
- Examination of uterine content: on day 20, gravid uterine weight, number of corpora lutea, number of implantations
- Examination of fetuses: on day 20, litter size, number of dead fetuses, fetal weight, sex ratio, grossly visible/external abnormalities

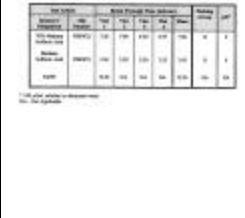
|                                  |   |  |
|----------------------------------|---|--|
| <b>Test substance</b>            | : | Test article name: Methanesulfonic acid<br>CAS no. : 75-75-2<br>Source: Elf atochem<br>Batch number: C06G<br>Purity: 70.15% in water   |
| <b>Conclusion</b>                | : | Maternal toxicity was observed at dose levels of 100, 200 and 300 mg/kg/d (administered at a concentration of 50 mg/ml), as evidenced by changes in the clinical condition of the animals and inhibition of body weight gain and food consumption.<br>No maternal toxicity was observed at dose levels of 25 and 50 mg/kg/d (administered at a concentration of 25 mg/ml).<br>No developmental toxicity was observed at dose levels up to 300 mg/kg/d. |
| <b>Reliability</b><br>17.03.2006 | : | (1) valid without restriction  |

(13)

## 5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

## 5.9 SPECIFIC INVESTIGATIONS

|                                |   |  |
|--------------------------------|---|--|
| <b>Endpoint</b>                | : | other: corrosivity test  |
| <b>Study descr. in chapter</b> | : |  |
| <b>Reference</b>               | : |  |
| <b>Type</b>                    | : | other: in vitro  |
| <b>Species</b>                 | : |  |
| <b>Sex</b>                     | : |  |
| <b>Strain</b>                  | : |  |
| <b>Route of admin.</b>         | : |  |
| <b>No. of animals</b>          | : |  |
| <b>Vehicle</b>                 | : | water  |
| <b>Exposure period</b>         | : | 4 hour(s)  |
| <b>Frequency of treatm.</b>    | : | single exposure  |
| <b>Doses</b>                   | : |  |
| <b>Control group</b>           | : | yes  |
| <b>Observation period</b>      | : | 4 hours  |
| <b>Result</b>                  | : | 7min02 (70% methane sulfonic acid) and 3min43 (methane sulfonic acid). |
| <b>Method</b>                  | : |  |
| <b>Year</b>                    | : |  |
| <b>GLP</b>                     | : | no   |
| <b>Test substance</b>          | : |  |
| <b>Remark</b>                  | : | study peer reviewed  |
| <b>Result</b>                  | : | RESULTS OF PILOT STUDY:  |

- Qualification screen allows CDS use.  
Categorization screen allows using the following scoring scale:  
Up to 3 minutes: Corrosive (Packing group I)  
>3 min but <1h: Corrosive (Packing group II)  
>1h but <4h: Corrosive (Packing group III)  
>4h: No corrosive
- Source** : ATOFINA, Paris-La Défense, France.  
Atofina Paris La Défense Cedex
- Test condition** : PRINCIPLE OF THE TEST:  
The Corrositex assay is used as a standardized and quantitative in vitro corrosivity test. The test is based on the time that is required for the test sample to pass through a biobarrier membrane and produce a change in the Chemical Detection System (CDS).
- MATERIAL AND METHOD:**  
- Biobarrier: membrane disc (unknown composition) placed in a scintillation vial above a chemical detection system.  
- Chemical Detection System: unknown composition  
- Volume or quantity administered: 500 µl  
- Negative control: distilled water  
- Positive control: sodium hydroxyde  
- number of replicates: 4  
- Experiment schedule: Once test substance is placed on membrane disc, vials are continuously observed for the first 10 minutes and then at approximately 5 minutes intervals for up to 4 hours.  
- Measured parameter: time is recorded from test substance application until CDS colour change.  
- Pilot study: Yes
- A preliminary study was conducted in order to determine whether test substance can be detected by CDS or not (qualification screen) and whether the schedule and scoring scale are adapted to the test substance (categorization screen). Methods of such preliminary test are not available.
- Test substance** : Test article name: Methanesulfonic acid 70%  
CAS no. : 75-75-2  
Source: Elf Atochem NA  
Batch no.: not specified  
Purity: 69.9% in water  
Test article name: Methanesulfonic acid anhydrous  
CAS no. 75-75-2  
Source: Elf Atochem NA  
Batch number: L06F  
Purity: 99.87%
- Attached document** : 75-75-2 Corrosivity test.bmp
- 
- Conclusion** : This in vitro test allows to consider METHANE SULFONIC ACID (anhydrous and 70% diluted) as corrosive with regard to biomembranes.
- Reliability** : (2) valid with restrictions

## 5. Toxicity

**Id** 75-75-2  
**Date** 10.10.2006

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**Flag** : Material Safety Dataset, Directive 67/548/EEC  
31.08.2005 (18)

### 5.10 EXPOSURE EXPERIENCE

### 5.11 ADDITIONAL REMARKS

**6.1 ANALYTICAL METHODS**

**6.2 DETECTION AND IDENTIFICATION**

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**7.1 FUNCTION**

**7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED**

**7.3 ORGANISMS TO BE PROTECTED**

**7.4 USER**

**7.5 RESISTANCE**

**8.1 METHODS HANDLING AND STORING**

**8.2 FIRE GUIDANCE**

**8.3 EMERGENCY MEASURES**

**8.4 POSSIB. OF RENDERING SUBST. HARMLESS**

**8.5 WASTE MANAGEMENT**

**8.6 SIDE-EFFECTS DETECTION**

**8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER**

**8.8 REACTIVITY TOWARDS CONTAINER MATERIAL**

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**Id** 75-75-2  
**Date** 10.10.2006

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## 10.1 END POINT SUMMARY

## 10.2 HAZARD SUMMARY

**Chapter** : Environmental Fate and Pathways

**Source** : Atofina Paris La Défense Cedex

**Conclusion** : Methanesulfonic acid is considered as readily biodegradable in an 301 A DOC Die-away, with 100% biodegradation within 28 day.

As shown in an OECD 303 A, methane sulfonic acid presents a good biodegradation potential in a waste water treatment plant, but only if it arrives steadily at the plant. Actually, sludge adaptation time was found to be very long here. This means ponctual rejects would probably not be treated.

It is expected to be not bioaccumulable with a negative n-octanol / water partition coefficient log Kow = -4.98.

07.03.2003

**Chapter** : Ecotoxicity

**Source** : Atofina Paris La Défense Cedex

**Conclusion** : Methanesulfonic acid has been shown to be slighly harmful to microcrustacea (Daphnia magna) with an EC50,48h > 100 mg/l, at pH 6.4.

An EC50, 24h of pH 3.5 was obtained, giving a substance concentration of 1.7 mg/l.

The substance is harmful to fish, with an LC50 96h in the range 10-100 mg/l, at pH approximatively 7.

It was found to be harmful to aquatic flora (algae), with an EC50, 72h (growth rate and biomass) ranging from 1 to 10 mg/l, at pH 7.5.

07.03.2003

**Chapter** : Toxicity

**Result** : Acute oral toxicity studies in rats with methanesulfonic acid have resulted in LD50's of 649 mg/kg for the anhydrous form and 1157 mg/kg for the 70% solution. Dermal LD50 is estimated to be between 200 and 2000 mg/kg in rabbits. No toxicity was found after an acute exposure to methane sulfonic acid saturated atmosphere. This phenomenon is probably due to the slight volatility of this compound. Methane sulfonic acid is corrosive to rabbit skin and eye. However, no sensitization has been detected in guinea pigs. Exposure of albino rats to an aerosol of methane sulfonic acid for 4 weeks resulted in changes in the clinical conditions of the animals at exposure levels of 0.073 and 0.242 mg/L, a transient reduced mean body weight gain in the 0.242 mg/L exposure level males, slightly reduced food consumption means in the 0.242 mg/L exposure level males and histopathologic lesions in the nasal turbinates of all exposed groups. Based on the data obtained during the two-week recovery (nonexposure) period, the effects on the

clinical conditions of the animals and body weight gains were completely reversible; histopathological lesions in the nasal turbinates were observed in all groups at the end of the recovery period. Based on the compound-induced lesions observed in the nasal turbinates, the no observed effect level (NOEL) for local irritation was considered to be less than 0.026 mg/L. The NOEL for systemic toxicity was considered to be 0.026 mg/L. In contrast, a 7-day oral exposure did not induced any toxic effects, so that NOEL was valued at 1805 mg/kg for males and 2122 mg/kg for females. Methanesulfonic acid was not genotoxic in bacterial reverse mutations assays and in the bone marrow micronucleus assay in mice.

In an oral developmental toxicity study in rats, a dose level of 400 mg/kg/day was considered to be the no observable adverse effect level (NOAEL) for maternal toxicity and developmental toxicity of Methane Sulfonic Acid.

**Source**  
07.03.2003

: Atofina Paris La Défense Cedex

### 10.3 RISK ASSESSMENT

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**TABLE 1: DATA ANALYSIS/TESTING FOR MSA (CAS# 75-75-2)**

| CAS No.: 75-75-2  | Results  | Reliability <sup>1</sup> | Result of Data Review/<br>Proposed Data Development | References                         |
|---|--|--------------------------|---|------------------------------------|
| <b>PHYSICAL/CHEMICAL DATA</b>   |  |                          |   |                                    |
| Melting Point   | 19°C   | 2                        | Data Adequate/No testing                            | Elf Atochem, 1987                  |
| Boiling Point   | 167°C @ 13hPa  | 2                        | Data Adequate/No Testing                            | Merck Index, 1989                  |
| Vapor Pressure  | 0.013 hPa @ 20°C   | 2                        | Data Adequate/No Testing                            | Elf Atochem, 1994                  |
| Partition Coefficient<br>(Octanol/Water)                              | -4.98  | 2                        | Data Adequate/No Testing                            | Leo, 1978                          |
| Water Solubility  | 1000 g/ml  | 2                        | Data Adequate/No Testing                            | ATOFINA, 1987, Lewis. 1993         |
| <b>ENVIRONMENTAL FATE AND PATHWAY</b>                                 |  |                          |   |                                    |
| Aerobic Biodegradability  | 100% after 28 days   | 1                        | Adequate Data / No Testing                          | Elf Atochem, 1995                  |
| Abiotic Hydrolysis  |  |                          | Technical Discussion Proposed                       |                                    |
| Photodegradability  | t <sub>1/2</sub> = 38.75 Days                              | 2                        | Adequate Data / No Testing                          | EPIWIN v 3.10                      |
| Estimates of Environmental<br>Fate<br>(Fugacity Model – Level<br>III) | Air: 0.4%<br>Water: 45.6%<br>Soil: 54 %<br>Sediment: <0.1% | 2                        | Adequate Data / No Testing                          | EPIWIN v3.10                       |
| <b>ECOTOXICOLOGY DATA:</b>  |  |                          |   |                                    |
| Acute Toxicity to Fish  | 73 mg/l  | 1                        | Adequate Data / No Testing                          | Elf Atochem, 1998                  |
| Acute Toxicity to Daphnids  | 260 mg/l   | 1                        | Adequate Data / No Testing                          | Elf Atochem, 1998                  |
| Acute Toxicity to Algae   | 14   | 1                        | Adequate Data / No Testing                          | Elf Atochem, 199                   |
| <b>TOXICOLOGY DATA:</b>   |  |                          |   |                                    |
| Acute Toxicity<br>Oral (anhydrous)                                    | LD50= 649 mg/kg  | 1                        | Adequate Data / No Testing                          | Elf Atochem, 1998                  |
| Dermal (70%)  | LD50 > 1000 mg/kg  | 1                        | Adequate Data / No Testing                          | Elf Atochem, 2002                  |
| Repeated Dose Toxicity<br>OECD 407                                    | NOAEL = 0.026 mg/l   | 1                        | Adequate Data / No Testing                          | Elf Atochem, 1996                  |
| Genetic toxicity<br><i>Mutagenicity (Ames test)</i>                   | Negative   | 1                        | Adequate Data / No Testing                          | Elf Atochem, 1990<br>Penwalt, 1989 |
| <i>Chromosomal Effects<br/>(micronucleus)</i>                         | Negative   | 1                        | Adequate Data / No Testing                          | Penwalt, 1989                      |
| Developmental Toxicity<br>OECD 414                                    | NOAEL > 400 mg/kg <sup>2</sup>                             | 1                        | Adequate Data / No Testing                          | Elf Atochem, 1996                  |
| Reproductive Toxicity   | No Data  |                          | Testing Proposed (OECD 408)                         |                                    |

<sup>1</sup> All data were evaluated for study reliability in accordance with criteria outlined by USEPA (*Determining the Adequacy of Existing Data*. OPPT, EPA, 1999).

<sup>2</sup> - highest dose tested

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