



Name: OECD_SIDS / SUBSTANCE : 2,4-Dimethylbenzenesulfonic acid / 2,4-dimethylbenzenesulfonic acid / 88-61-9 Tue, 29 Nov 2022, 15:15:34+0900 /

Legal entity owner: National Institute of Health Science

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Author:

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Remarks:

Dossier header

Dossier submission type

Name

OECD SIDS

Version

core 7.0

Name (given by user)

Dossier subject

Dossier subject

[2,4-Dimethylbenzenesulfonic acid / 2,4-dimethylbenzenesulfonic acid / 88-61-9](#)

Public name

Submitting legal entity

[National Institute of Health Science](#)

Dossier creation date/time

Tue, 29 Nov 2022, 15:15:34+0900

Used in category

LEGAL_ENTITY: National Institute of Health Science

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Remarks:

General information

Legal entity name

National Institute of Health Science

2,4-Dimethylbenzenesulfonic acid

General information

Identification

Identification

SUBSTANCE: 2,4-Dimethylbenzenesulfonic acid

UUID: f37cc151-6c6c-4e4a-8f63-01f344b6b8eb

Dossier UUID:

Author:

Date: 2022-11-29T15:08:23.069+09:00

Remarks:

Substance name

2,4-Dimethylbenzenesulfonic acid

Legal entity

[National Institute of Health Sciences / Kawasaki / Japan](#)

Identification of substance

Reference substance

[m-xylene-4-sulphonic acid / 2,4-dimethylbenzenesulfonic acid / 88-61-9 / 201-843-9](#)

EC number

201-843-9

EC name

EC Inventory

CAS number

88-61-9

CAS name

IUPAC name

2,4-dimethylbenzenesulfonic acid

Role in the supply chain

Manufacturer

false

Importer

false

Only representative

false

Downstream user

false

Toxicological information

Repeated dose toxicity

Repeated dose toxicity: oral

ENDPOINT_STUDY_RECORD: Repeated dose toxicity: oral.001

UUID: 03fc6df8-c0f1-4273-a0bd-e15545463b81

Dossier UUID:

Author:

Date: 2022-11-29T15:08:23.069+09:00

Remarks:

Administrative data

Endpoint

short-term repeated dose toxicity: oral

Type of information

experimental study

Adequacy of study

key study

Robust study summary

false

Used for classification

false

Used for SDS

false

Reliability

1 (reliable without restriction)

Rationale for reliability incl. deficiencies

other: OECD Test Guideline study under GLP condition

Cross-reference

Reason / purpose for cross-reference

reference to same study 7.8.1 Toxicity to reproduction: Toxicity to reproduction. 001

Related information

[OECD / Toxicity to reproduction / Toxicity to reproduction.001 / 2,4-Dimethylbenzenesulfonic acid / 2,4-dimethylbenzenesulfonic acid / 88-61-9](#)

Data source

Reference

[Combined repeated dose toxicity study with the reproductive/developmental toxicity screening test of / Ministry of Health, Labour and Welfare \(MHLW\), Japan / study report](#)

Data access

data published

Materials and methods

Test guideline

Qualifier

according to guideline

Guideline

OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test)

Deviations

yes During the power outage (October 2, 2010) due to the inspection of the electrical equipment of the facility, the humidity increased (78%), the lights were turned off, and the ventilation was stopped.

However, no effect was observed on the test results.

GLP compliance

yes

Limit test

no

Test material

Test material information

[2,4-Dimethylbenzenesulfonic acid](#)

Specific details on test material used for the study

- Name of test material (as cited in study report): 2,4-Dimethylbenzenesulfonic acid
- Analytical purity: 99.7% (anhydrous equivalent, contained 16.1% water)
- Storage condition of test material: Room temperature, shading
- Stability under test conditions: The stability of test material was identified by analysis of the remainder.

Test animals

Species

rat

common rodent species

Strain

other: Crl:CD(SD)

Sex

male/female

Details on test animals or test system and environmental conditions**TEST ANIMALS**

- Source: Charles River Japan, Inc., Atsugi Breeding Center.
- Age at study initiation: 10 weeks old
- Weight at study initiation:
Male: 355-428 g, Female: 220-249 g
- Housing:
Mating period: Stainless steel mesh cages for group housing (340W × 294D × 176H mm)
After 18 days of pregnancy: Stainless steel cage for delivery (340W × 294D × 176H mm) and bedding.
Other breeding period: 2-piece stainless steel mesh cage (170W × 294D × 176H mm/animal)
- Diet: Solid feed (CRF-1: Oriental Yeast Co., Ltd.) was given ad libitum.

-
- Water: Tap water was given ad libitum.
 - Acclimation period: 15 days

ENVIRONMENTAL CONDITIONS

- Temperature (°C): 23±2°C (actual temperature: 21.9-24.1°C)
- Humidity (%): 55±15% (actual humidity: 52-78%)
- Air changes (per hr): 15-17
- Photoperiod (hrs dark / hrs light): 12 hr dark/12 hr light (light: 8:00~20:00)

Administration / exposure

Route of administration

oral: gavage

Vehicle

water for injection

Details on oral exposure

- Amount of vehicle (if gavage): 5 mL/kg
- Dosing volume: 5 mL/kg

Analytical verification of doses or concentrations

yes

Details on analytical verification of doses or concentrations

Concentrations of the test solutions at the time of initial preparation were analyzed with HPLC. Analytical concentrations of the test solutions were all within the range of 96.0-98.5% of the nominal concentrations and both values were within the acceptable range.

Duration of treatment / exposure

Males: 42 days including 14 days pre-mating, 14 days mating period and 14 days after the end of the mating period.

Females (mating): 42-46 days including 14 days pre-mating, mating and gestation periods and the days until day 4 of lactation. (no mating females: 41-43 days)

Females (satellite): 42 days

Frequency of treatment

Once/day, 7 days/week

Doses / concentrations

Dose / conc.	
0	mg/kg bw/day (actual dose received)
Dose / conc.	
20	mg/kg bw/day (actual dose received)
Dose / conc.	
100	mg/kg bw/day (actual dose received)

Dose / conc.

500 mg/kg bw/day (actual dose received)

No. of animals per sex per dose

Mating group: 12 animals/sex /dose (0, 20, 100, and 500 mg/kg bw/day). 5 males at 0 and 500 mg/kg bw/day were assigned to the recovery group.

Non-mating group (Satellite group): 10 females/dose (0 and 500 mg/kg bw/day). 5 females at each group were assigned to the recovery group.

Control animals

yes, concurrent vehicle

Details on study design

- Dose selection rationale: Based on the results of a 14-day preliminary study, the high dose was set to 500 mg/kg bw/day, and the intermediate dose and low dose were set to 100 mg/kg bw/day and 20 mg/kg bw/day, respectively.

[14-day preliminary study]

A 14-day repeated dose oral toxicity test (CrI:CD(SD) rats, doses: 0, 100, 300, 600 or 1000 mg/kg bw/day).

A moribund condition with dyspnea was seen in 1 male at 1000 mg/kg bw/day and 1 female at 600 mg/kg bw/day and was killed as impending. In males and females at 1000 mg/kg bw/day, irregular respiration was observed. In males and females at 600 mg/kg bw/day and above, decrease in body weight and food consumption, swelling of stomach wall were observed.

- Rationale for animal assignment (if not random): Body weight-balanced randomization

Examinations**Observations and examinations performed and frequency**

CAGE SIDE OBSERVATIONS: Yes

- Time schedule:

2 times/day (before administration, after administration) during the administration period. Once a day during the recovery period.

DETAILED CLINICAL OBSERVATIONS: Yes

- Time schedule:

Male:

Detailed observation was conducted weekly during the administration and recovery periods.

Reactivity test, grip strength measurement, and motor activity measurement were performed once every 6 weeks after administration.

Female:

Detailed observation was conducted weekly during the administration and recovery periods. However, only the satellite group was observed for 6 weeks after administration.

Reactivity test, grip strength measurement, and motor activity measurement were performed on the day before anatomy in the parturition animals and once every 6 weeks in the satellite group.

BODY WEIGHT: Yes

- Time schedule for examinations:

Males, females (satellite):

On days 1, 8, 15, 22, 29, 36, and 42 of administration period. On days 1, 8 and 14 of recovery period.

Females (mating):

Before mating, measurements were taken on days 1, 8 and 15 of administration. Mated females were measured at gestation 0, 7, 14, and 20. The delivered females were measured on the day of delivery and 4 days after delivery.

FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):

- Food consumption: Yes

- Time schedule for examinations:

Males, females (satellite):

On days 1, 8, 15, 29, 36, 42 of administration period.

On days 1, 8, 14 of recovery period.

Females (mating):

On days 1, 8, 15 of administration period, on days 0, 7, 14, 20 of gestation period, on days 0, 4 of lactation period.

WATER INTAKE: No

OPHTHALMOSCOPIC EXAMINATION: No

HAEMATOLOGY: Yes

- Time schedule for collection of blood:

At the end of administration period, or at the end of recovery period in both sexes

- Anaesthetic used for blood collection: ether

- Animals fasted: Yes

- How many animals:

At the end of administration period:

Males: 7, 12, 12, and 7 males/dose (0, 20, 100, and 500 mg/kg bw/day)

Females (mating): 12 females/dose (0, 20, 100, and 500 mg/kg bw/day),

Females (satellite): 5 females/dose (0 and 500 mg/kg bw/day)

At the end of recovery period:

5 males/dose and 5 females (satellite)/dose (0 and 500 mg/kg bw/day)

- Parameters examined: red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, reticulocyte percentage, platelet count, white blood cell count, differential white blood cell count, prothrombin time, activated partial thromboplastin time.

CLINICAL CHEMISTRY: Yes

- Time schedule for collection of blood:

At the end of administration period, or at the end of recovery period in both sexes

- Animals fasted: Yes

- How many animals:

At the end of administration period:

Males: 7, 12, 12, and 7 males/dose (0, 20, 100, and 500 mg/kg bw/day)

Females (mating): 12 females/dose (0, 20, 100, and 500 mg/kg bw/day),

Females (satellite): 5 females/dose (0 and 500 mg/kg bw/day)

At the end of recovery period:

5 males/dose and 5 females (satellite)/dose (0 and 500 mg/kg bw/day)

- Parameters checked: total protein, albumin, A/G ratio, total bilirubin, glucose, total cholesterol, triglyceride, phospholipid, AST, ALT, LDH, ALP, γ -GT, CK, BUN, creatinine, sodium, potassium, chloride, calcium, inorganic phosphorus

BLOOD HORMONE: Yes

- Time schedule for collection of serum:

At the end of administration period, or at the end of recovery period in both sexes

- Animals fasted: Yes

- How many animals:

At the end of administration period:

Males: 7, 12, 12, and 7 males/dose (0, 20, 100, and 500 mg/kg bw/day)

Females (mating): 12 females/dose (0, 20, 100, and 500 mg/kg bw/day),

Females (satellite): 5 females/dose (0 and 500 mg/kg bw/day)

At the end of recovery period:

5 males/dose and 5 females (satellite)/dose (0 and 500 mg/kg bw/day)

- Parameters checked: Triiodothyronine (T3), Thyroxin (T4), and thyroid stimulating hormone (TSH)

URINALYSIS: Yes

- Time schedule for collection of urine:

Male, female satellite group: Fresh urine was collected before administration once at week 6 of administration period.

- Metabolism cages used for collection of urine: No

A urine collector to collect fresh urine samples under ad libitum feeding and drinking conditions.

- How many animals:

At the end of administration period:

Male: 7, 12, 12, and 7 males/dose (0, 20, 100, and 500 mg/kg bw/day)

Females (satellite): 10 females/dose (0 and 500 mg/kg bw/day)

- Parameters checked:

Fresh urine: pH, protein, glucose, ketones, bilirubin, occult blood, urobilinogen

NEUROBEHAVIOURAL EXAMINATION: Yes

- Time schedule for examinations:

Males and females (satellite): Week 6 of administration period.

Females (mating): The animals were delivered on the day before dissection (4 days after delivery).

- Dose groups that were examined: Autopsy animals after the end of the administration period

- Battery of functions tested:

1) Reflex/reactions (Manipulative Test). Visual forelimb placing response, auditory reactivity, tail pinch response, pupillary reflex, aerial righting reaction.

2) Measurement of Grip Strength. Grip strength of forelimb and hind limb was measured by MK-380CM (Muromachi kikai Co.,Ltd.).

3) Measurement of Spontaneous Motor Activity. Spontaneous motor activity was measured by SCANET MV-10 (MELQUEST Ltd.).

Motor activity was measured for 60 min.

Sacrifice and pathology

GROSS PATHOLOGY: Yes

ORGAN WEIGHT: Yes

: pituitary, thyroids, heart, liver, kidney, thymus, spleen, adrenal gland, testes, epididymides, ventral prostate, seminal vesicles (including coagulating gland) , ovaries, uterus, brain, lung

HISTOPATHOLOGY: Yes: brain. pituitary, spinal cord, eye ball, thyroid, parathyroid, heart, nasal cavity, trachea, lung, liver, kidney, thymus, spleen, adrenal glands, stomach, small intestine (including duodenum), large intestine, testis, epididymis, ventral prostate, seminal vesicles (including coagulating gland), ovaries, uterus, vagina, urinary bladder, lymph nodes (axillary, inguinal, etc.), peripheral nerve (sciatic nerve), bone marrows (femur), bone (femur), mammary gland, muscle.

Statistics

For population index, fertility index, gestation index, urinalysis and histopathological findings, statistical difference between each treatment group and the control group was analyzed using by the Chi-square test.

For quantitative data, homogeneity of variance was tested using Bartlett method first. If the variance was homogenous, statistical difference between each treatment group and the control group was analyzed using Dunnett method. If not homogenous, statistical difference between each treatment group and the control group was tested using Kurskal-Wallis rank sum test and the significant difference between the medium control and treated groups was analyzed by nonparametric Dunnett multiple comparison test. For comparison of quantitative data between two groups in female satellite animals and male recovery test, homogeneity of variance was analyzed by F-test. Then, if homogenous, student's t-test was applied. If not homogenous, Aspin-Welch's t-test was used.

Results and discussion

Results of examinations

Clinical signs

effects observed, treatment-related

Description (incidence and severity)

CLINICAL SIGNS:

[At the administration period]:

Abnormal respirations (males and females: respiratory noise, irregular respiration, females: oral breathing) were observed in males and females at 500 mg/kg bw/day. Soiled perigenital region was observed in females at 500 mg/kg bw/day.

[At the recovery period]:

Deep respiration was observed in males at 500 mg/kg bw/day.

DETAILED CLINICAL OBSERVATIONS:

[At the administration period]:

Abnormal respiration (males and females: respiratory noise, males: irregular respiration), and soiled perinasal were observed in males and females at 500 mg/kg bw/day.

[At the recovery period]

Deep respiration, soiled perigenital region and low temperature of the skin were observed in males at 500 mg/kg bw/day.

Mortality

mortality observed, non-treatment-related

Description (incidence)

One female in the satellite group at 500 mg/kg bw/day died on day 10. In this fatal case, erosion and inflammation in the larynx through the upper part of the trachea were observed. Obstruction in the upper trachea by pus and congestion/edema of the lung were also observed, suggesting that the cause of death was suffocation in this female. To investigate obstruction in the nasal cavity, a detailed histopathological examination in the nasal mucosa of all animals was conducted; however, there were no lesions causing obstruction in any animal. An intubation error could not be excluded as the cause of death. Therefore, this death was treatment-related but was not toxicologically relevant.

Body weight and weight changes

effects observed, treatment-related

Description (incidence and severity)

[At the administration period]:

Decreased tendency body weight gain was observed in males at 500 mg/kg bw/day.

[At the recovery period]:

Decreased tendency body weight gain was observed in males at 500 mg/kg bw/day.

Food consumption and compound intake (if feeding study)

no effects observed

Food efficiency

not examined

Water consumption and compound intake (if drinking water study)

not examined

Ophthalmological findings

not examined

Haematological findings

not specified

Description (incidence and severity)

[At the end of administration period]:

Decreased MCH was observed in males at 500 mg/kg bw/day. This finding was not associated with other changes and was confined to the highest dose and no longer apparent after the recovery period. This change may be treatment related but were not necessarily adverse.

[At the end of recovery period]:

There were no changes related to the test substance in any groups.

Clinical biochemistry findings

not specified

Description (incidence and severity)

Including blood hormones (T3, T4, TSH)

CLINICAL BIOCHEMISTRY:

[At the end of administration period]:

Decreased total protein and albumin were observed in males at 500 mg/kg bw/day. Decreased BUN creatinine and IP were observed in mating females at 500 mg/kg bw/day. Decreased total protein, increased AST were observed in satellite females at 500 mg/kg bw/day.

These findings were not associated with other signs, organ weight changes, or histopathological alterations and were confined to the highest dose and no longer apparent after the recovery period.

These changes may be treatment related but were not necessarily adverse.

[At the end of recovery period]:

There were no changes related to the test substance in any groups.

BLOOD HORMONES:

There were no changes related to the test substance in any groups at the administration and recovery periods.

Urinalysis findings

no effects observed

Behaviour (functional findings)

no effects observed

Immunological findings

not examined

Organ weight findings including organ / body weight ratios

no effects observed

Gross pathological findings

no effects observed

Neuropathological findings

not examined

Histopathological findings: non-neoplastic

no effects observed

Histopathological findings: neoplastic

not examined

Effect levels

Key result

true

Dose descriptor

NOAEL

Effect level

100

mg/kg bw/day (actual dose received)

Based on

test mat.

Sex

male/female

Basis for effect level

clinical signs

At 500 mg/kg bw/day, abnormal respiration was observed in males and females.

Any other information on results incl. tables

Figures and Tables (in English) are available in the following full report of the study.
https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF88-61-9d.pdf

Applicant's summary and conclusion**Conclusions**

Based on the changes in the clinical sign, the NOAEL of repeated dose toxicity was determined to be 100 mg/kg bw/day in male and female rats.

Executive summary

In the combined repeated dose and reproductive/developmental screening test (OECD TG422), SD rats were treated orally with the test substance at the doses of 0, 20, 100 and 500 mg/kg bw/day. Males (12 animals/dose) were dosed for 42 days including a 14 day pre-mating period. Females (12 animals/dose) were dosed for 41-46 days including 14 day pre-mating, mating, and gestation periods and days until day 4 of lactation. In addition, as the satellite study group of females (10 females/group) was dosed 0 and 500 mg/kg/day for 42 days, with 5 animals/group treated with recovery.

Irregular respiration, deep respiration, and dyspnea, which were considered to represent main toxic effects, were observed in males and females at the 500 mg/ kg bw/day. Decreased tendency body weight gain was observed in males at 500 mg/kg bw/day. In the hematological examination, decreased MCH was observed in males at 500 mg/kg bw/day. In the clinical chemistry, decreased total protein and albumin in males, decreased BUN, creatinine and IP in mating females, decreased total protein, and increased AST in satellite females were observed at 500 mg/kg bw/day. These findings were not associated with other signs, organ weight changes, or histopathological alterations and were confined to the highest dose and no longer apparent after the recovery period. These changes may be treatment related but were not necessarily adverse.

Since respiratory abnormalities were observed at 500 mg/kg bw/day for both sexes, The NOAELs for repeated dose toxicity of 2,4-dimethylbenzenesulfonic acid were determined to be 100 mg/kg bw/day in male and female rats.

Genetic toxicity

Genetic toxicity in vitro

ENDPOINT_STUDY_RECORD: Genetic toxicity in vitro.001

UUID: 4ea32234-fc9e-469a-af00-29d60f718f20

Dossier UUID:

Author:

Date: 2022-11-14T14:51:43.000+09:00

Remarks:

Administrative data

Endpoint

in vitro gene mutation study in bacteria

Type of information

experimental study

Adequacy of study

key study

Robust study summary

false

Used for classification

false

Used for SDS

false

Reliability

1 (reliable without restriction)

Rationale for reliability incl. deficiencies

guideline study under GLP condition

Reliability 1

Data source

Reference

[Reverse Mutation Test of 2,4-Dimethylbenzenesulfonic acid on Bacteria. / Ministry of Health, Labour and Welfare \(MHLW\), Japan / study report](#)

Data access

data published

Materials and methods

Test guideline

Qualifier

according to guideline

Guideline

OECD Guideline 471 (Bacterial Reverse Mutation Assay)
in vitro gene mutation study in bacteria

Deviations

no

Qualifier

according to guideline

Guideline

JAPAN: Guidelines for Screening Mutagenicity Testing Of Chemicals
genetic toxicity in vitro, other

Deviations

no

GLP compliance

yes

Type of assay

bacterial reverse mutation assay
in vitro gene mutation study in bacteria

Test material**Test material information**

[2,4-Dimethylbenzenesulfonic acid](#)

Specific details on test material used for the study

Purity: 99.7% (anhydrous equivalent, contained 16.1% water)

Method**Species / strain****Species / strain / cell type**

S. typhimurium TA 1535, TA 1537, TA 98 and TA 100
bacteria

Species / strain / cell type

E. coli WP2 uvr A pKM 101
bacteria

Metabolic activation

with and without

Metabolic activation system

S9 mix: SD male rat liver, induced by phenobarbital and 5,6-benzoflavone

Test concentrations with justification for top dose

-S9 mix:

313, 625, 1250, 2500, 5000 µg/plate (TA 1535, TA 1537, TA 98 and TA 100 strains)

313, 625, 1250, 2500, 5000 µg/plate (WP2uvrA/pKM101 strain)

+S9 mix (10%):

313, 625, 1250, 2500, 5000 µg/plate (TA 1535, TA 1537, TA 98 and TA 100 strains)

313, 625, 1250, 2500, 50000 µg/plate (WP2uvrA/pKM101 strain)
+S9 mix (30%):
313, 625, 1250, 2500, 5000 µg/plate (TA 1535, TA 1537, TA 98 and TA 100 strains)
313, 625, 1250, 2500, 50000 µg/plate (WP2uvrA/pKM101 strain)

Maximum concentration was established based on the result of the preliminary test at concentration up to 5000 µg/plate. In this test, the growth inhibition was not observed for all strains with or without S9 mix.

Vehicle / solvent

- Vehicle(s)/solvent(s) used: Distilled water

Controls

Untreated negative controls

no

Negative solvent / vehicle controls

yes

True negative controls

no

Positive controls

yes

Positive control substance

9-aminoacridine

9-aminoacridine hydrochloride (9AA): -S9 mix: (TA1537)

sodium azide

NaN₃: -S9 mix: (TA1535)

furylfuramide

2-(2-Furyl)-3-(5-nitro-2-furyl) acrylamide (AF-2): -S9 mix: (TA100, TA98, WP2 uvrA/pKM101)

other: 2-aminoanthracene (2AA)

+S9 mix: (TA1535, TA100, TA98, TA1537 and WP2 uvrA/pKM101)

Details on test system and experimental conditions

METHOD OF APPLICATION: Preincubation

DURATION- Preincubation period: 20 min at 37°C

- Exposure duration: ca.48 hrs

NUMBER OF PLATES: 3

NUMBER OF REPLICATIONS: 2

DETERMINATION OF CYTOTOXICITY

- Method: other: growth inhibition

Evaluation criteria

A chemical was judged to be mutagenic when the mean number of revertant colonies per plate increased more than twice that of the negative control and when the dose-related and reproducible increase was observed.

Statistics

no

Results and discussion

Test results**Key result**

true

Species / strainS. typhimurium TA 1535
bacteria**Metabolic activation**

with and without

Genotoxicity

negative

Cytotoxicity / choice of top concentrations

no cytotoxicity

Vehicle controls validity

valid

Untreated negative controls validity

not examined

True negative controls validity

not examined

Positive controls validity

valid

Key result

true

Species / strainS. typhimurium TA 1537
bacteria**Metabolic activation**

with and without

Genotoxicity

negative

Cytotoxicity / choice of top concentrations

no cytotoxicity

Vehicle controls validity

valid

Untreated negative controls validity

not examined

True negative controls validity

not examined

Positive controls validity

valid

Key result

true

Species / strain

S. typhimurium TA 98
bacteria

Metabolic activation

with and without

Genotoxicity

negative

Cytotoxicity / choice of top concentrations

no cytotoxicity

Vehicle controls validity

valid

Untreated negative controls validity

not examined

True negative controls validity

not examined

Positive controls validity

valid

Key result

true

Species / strain

S. typhimurium TA 100
bacteria

Metabolic activation

with and without

Genotoxicity

negative

Cytotoxicity / choice of top concentrations

no cytotoxicity

Vehicle controls validity

valid

Untreated negative controls validity

not examined

True negative controls validity

not examined

Positive controls validity

valid

Key result

true

Species / strain

E. coli WP2 uvr A pKM 101
bacteria

Metabolic activation

with and without

Genotoxicity

negative

Cytotoxicity / choice of top concentrations

no cytotoxicity

Vehicle controls validity

valid

Untreated negative controls validity

not examined

True negative controls validity

not examined

Positive controls validity

valid

Any other information on results incl. tables

Figures and Tables (in Japanese) are available in the following full report of the study.
https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF88-61-9e.pdf

Please also see the attached files (Tables in English)

Applicant's summary and conclusion**Conclusions**

Negative with or without metabolic activation

Executive summary

In a bacterial reverse mutation assay using *Salmonella typhimurium* TA100, TA1535, TA98, and TA 1537, and *Escherichia coli* WP2uvrA/pKM101 (OECD TG 471), 2,4-Dimethylbenzenesulfonic acid was negative with or without metabolic activation.

ENDPOINT_STUDY_RECORD: Genetic toxicity in vitro.002

UUID: 240d6348-464c-478f-9217-9454e4f61bb3

Dossier UUID:

Author:

Date: 2022-11-14T14:54:55.000+09:00

Remarks:

Administrative data

Endpoint

in vitro cytogenicity / chromosome aberration study in mammalian cells

Type of information

experimental study

Adequacy of study

key study

Robust study summary

false

Used for classification

false

Used for SDS

false

Reliability

1 (reliable without restriction)

Rationale for reliability incl. deficiencies

guideline study under GLP condition

Reliability 1

Data source

Reference

[In Vitro Chromosomal Aberration Test of on 2,4-Dimethylbenzenesulfonic acid Cultured Chinese Hamster / Ministry of Health, Labour and Welfare \(MHLW\), Japan / study report](#)

Data access

data published

Materials and methods

Test guideline

Qualifier

according to guideline

Guideline

OECD Guideline 473 (In Vitro Mammalian Chromosomal Aberration Test)

in vitro cytogenicity / chromosomal aberration study in mammalian cells (from 26 September 2014)

Deviations

no

Qualifier

according to guideline

GuidelineJAPAN: Guidelines for Screening Mutagenicity Testing Of Chemicals
genetic toxicity in vitro, other**Deviations**

no

GLP compliance

yes

Type of assayin vitro mammalian chromosome aberration test
in vitro cytogenicity / chromosome aberration study in mammalian cells

Test material**Test material information**[2,4-Dimethylbenzenesulfonic acid](#)**Specific details on test material used for the study**

Purity: 99.7% (anhydrous equivalent, contained 16.1% water)

Method**Species / strain****Species / strain / cell type**Chinese hamster lung (CHL/IU)
mammalian cell line**Cytokinesis block (if used)**

colcemid

Metabolic activation

with and without

Metabolic activation system

S9 mix: SD male rat liver, induced by phenobarbital and 5,6-benzoflavone

Test concentrations with justification for top dose

Cell growth inhibition study

-S9 mix (short-term treatment): 0.015, 0.03, 0.059, 0.12, 0.24, 0.48, 0.95, 1.9 mg/mL

+S9 mix (short-term treatment): 0.015, 0.03, 0.059, 0.12, 0.24, 0.48, 0.95, 1.9 mg/mL

-S9 mix (continuous treatment, 24hr): 0.015, 0.03, 0.059, 0.12, 0.24, 0.48, 0.95, 1.9 mg/mL

-S9 mix (continuous treatment, 48hr): 0.015, 0.03, 0.059, 0.12, 0.24, 0.48, 0.95, 1.9 mg/mL

Preliminary study

-S9 mix (short-term treatment): 0.24, 0.48, 0.95, 1.9 mg/mL

+S9 mix (short-term treatment): 0.24, 0.48, 0.95, 1.9 mg/mL

-S9 mix (continuous treatment, 24hr): 0.24, 0.48, 0.95, 1.9 mg/mL

-S9 mix (continuous treatment, 48hr): 0.24, 0.48, 0.95, 1.9 mg/mL

Main study

-S9 (short-term treatment): 0.48, 0.95, 1.4, 1.9 mg/mL

+S9 (short-term treatment): 0.48, 0.95, 1.4, 1.9 mg/mL
-S9 mix (continuous treatment, 24hr): 0.48, 0.95, 1.4, 1.9 mg/mL
-S9 mix (continuous treatment, 48hr): 0.48, 0.95, 1.4, 1.9 mg/mL
Confirmation study
+S9 (short-term treatment): 0.95, 1.4, 1.9 mg/mL

Vehicle / solvent

- Vehicle(s)/solvent(s) used: Distilled water

Controls

Untreated negative controls

no

Negative solvent / vehicle controls

yes

True negative controls

no

Positive controls

yes

Positive control substance

benzo(a)pyrene

+S9

mitomycin C

-S9

Details on test system and experimental conditions

METHOD OF APPLICATION: Exposure duration: [short-term treatment]: 6 hrs + 20 hr, [continuous treatment]: 24 hrs or 48 hrs

SPINDLE INHIBITOR: Colcemid

STAIN: Giemsa stain (2.5 v/v%) for 12 min.

NUMBER OF REPLICATIONS: 2

NUMBER OF CELLS EVALUATED: 100 + 100 cells /concentration

DETERMINATION OF CYTOTOXICITY

- Method: relative total growth

Evaluation criteria

For the evaluation of the frequencies of structural aberrations and of polyploidy induced, the following criteria were employed. Appearance incidence of cell with chromosomal aberrations: Negative (-): less than 5%, Equivocal(\pm): 5% or more and less than 10%, Positive(+): 10% or more

Statistics

no

Results and discussion

Test results

Key result

true

Species / strain

Chinese hamster lung (CHL/IU)

mammalian cell line

Metabolic activation

with and without

Genotoxicity

negative

Cytotoxicity / choice of top concentrations

no cytotoxicity

Vehicle controls validity

valid

Untreated negative controls validity

not examined

True negative controls validity

not examined

Positive controls validity

valid

Any other information on results incl. tables

Figures and Tables (in Japanese) are available in the following full report of the study.
https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF88-61-9f.pdf

Please also see the attached files (Tables in English)

Applicant's summary and conclusion

Conclusions

Negative with or without metabolic activation

Executive summary

In an in vitro chromosomal aberration test using CHL/IU cells (OECD TG 473), 2,4-dimethylbenzenesulfonic acid was negative with or without metabolic activation.

Toxicity to reproduction

Toxicity to reproduction

ENDPOINT_STUDY_RECORD: Toxicity to reproduction.001

UUID: b99d415f-750a-4ed1-a267-347b52c101ac

Dossier UUID:

Author:

Date: 2022-11-29T14:06:17.424+09:00

Remarks:

Administrative data

Endpoint

reproductive toxicity, other Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test

Type of information

experimental study

Adequacy of study

key study

Robust study summary

false

Used for classification

false

Used for SDS

false

Reliability

1 (reliable without restriction)

Rationale for reliability incl. deficiencies

other: OECD Test Guideline study under GLP condition

Cross-reference

Reason / purpose for cross-reference

reference to same study 7.5.1 Repeated dose toxicity: oral: Repeated dose toxicity: oral. 001

Related information

[OECD / Repeated dose toxicity: oral / Repeated dose toxicity: oral.001 / 2,4-Dimethylbenzenesulfonic acid / 2,4-dimethylbenzenesulfonic acid / 88-61-9](#)

Data source

Reference

[Combined repeated dose toxicity study with the reproductive/developmental toxicity screening test of / Ministry of Health, Labour and Welfare \(MHLW\), Japan / study report](#)

Data access

data published

Materials and methods

Test guideline

Qualifier

according to guideline

Guideline

OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test)

Deviations

yes During the power outage (October 2, 2010) due to the inspection of the electrical equipment of the facility, the humidity increased (78%), the lights were turned off, and the ventilation was stopped.

However, no effect was observed on the test results.

GLP compliance

yes

Limit test

no

Test material

Test material information

[2,4-Dimethylbenzenesulfonic acid](#)

Specific details on test material used for the study

- Name of test material (as cited in study report): 2,4-Dimethylbenzenesulfonic acid
- Analytical purity: 99.7% (anhydrous equivalent, contained 16.1% water)
- Storage condition of test material: Room temperature, shading
- Stability under test conditions: The stability of test material was identified by analysis of the remainder.

Test animals

Species

rat

Strain

other: CrI:CD(SD)

Sex

male/female

Details on test animals or test system and environmental conditions**TEST ANIMALS**

- Source: Charles River Japan, Inc., Atsugi Breeding Center.
- Age at study initiation: 10 weeks old
- Weight at study initiation: Male: 355-428 g, Female: 220-249 g
- Housing:
 - Mating period: Stainless steel mesh cages for group housing (340W × 294D × 176H mm)
 - After 18 days of pregnancy: Stainless steel cage for delivery (340W × 294D × 176H mm) and bedding.
 - Other breeding period: 2-piece stainless steel mesh cage (170W × 294D × 176H mm/animal)
- Diet: Solid feed (CRF-1: Oriental Yeast Co., Ltd.) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation period: 15 days

ENVIRONMENTAL CONDITIONS

- Temperature (°C): 23±2°C (actual temperature: 21.9-24.1°C)
- Humidity (%): 55±15% (actual humidity: 52-78%)
- Air changes (per hr): 15-17
- Photoperiod (hrs dark / hrs light): 12 hr dark/12 hr light (light: 8:00~20:00)

Administration / exposure

Route of administration

oral: gavage

Vehicle

water for injection

Details on exposure

- Amount of vehicle (if gavage): 5 mL/kg
- Dosing volume: 5 mL/kg

Details on mating procedure

- M/F ratio per cage:1/1
- Length of cohabitation: up to 14 days
- Proof of pregnancy: vaginal plug / sperm in vaginal smear referred to as day 0 of pregnancy

Analytical verification of doses or concentrations

yes

Details on analytical verification of doses or concentrations

Concentrations of the test solutions at the time of initial preparation were analyzed with HPLC. Analytical concentrations of the test solutions were all within the range of 96.0-98.5% of the nominal concentrations and both values were within the acceptable range.

Duration of treatment / exposure

Males: 42 days including 14 days pre-mating, 14 days mating period and 14 days after the end of the mating period.

Females (mating): 42-46 days including 14 days pre-mating, mating and gestation periods and the days until day 4 of lactation. (no mating females: 41-43 days)

Females (satellite): 42 days

Frequency of treatment

Once/day, 7 days/week

Doses / concentrations

Dose / conc.	
0	mg/kg bw/day (actual dose received)
Dose / conc.	
20	mg/kg bw/day (actual dose received)

Dose / conc.	
100	mg/kg bw/day (actual dose received)
Dose / conc.	
500	mg/kg bw/day (actual dose received)

No. of animals per sex per dose

Mating group: 12 animals/sex /dose (0, 20, 100, and 500 mg/kg bw/day). 5 males at 0 and 500 mg/kg bw/day were assigned to the recovery group.

Non-mating group (Satellite group): 10 females/dose (0 and 500 mg/kg bw/day). 5 females at each group were assigned to the recovery group.

Control animals

yes, concurrent vehicle

Details on study design

- Dose selection rationale: Based on the results of a 14-day preliminary study, the high dose was set to 500 mg/kg bw/day, and the intermediate dose and low dose were set to 100 mg/kg bw/day and 20 mg/kg bw/day, respectively.

[14-day preliminary study]

A 14-day repeated dose oral toxicity test (CrI:CD(SD) rats, doses: 0, 100, 300, 600 or 1000 mg/kg bw/day).

A moribund condition with dyspnea was seen in 1 male at 1000 mg/kg bw/day and 1 female at 600 mg/kg bw/day and was killed as impending. In males and females at 1000 mg/kg bw/day, irregular respiration was observed. In males and females at 600 mg/kg bw/day and above, decrease in body weight and food consumption, swelling of stomach wall were observed.

- Rationale for animal assignment (if not random): Body weight-balanced randomization

Examinations

Parental animals: Observations and examinations

CAGE SIDE OBSERVATIONS: Yes

- Time schedule:

2 times/day (before administration, after administration) during the administration period. Once a day during the recovery period.

DETAILED CLINICAL OBSERVATIONS: Yes

- Time schedule:

Male:

Detailed observation was conducted weekly during the administration and recovery periods.

Reactivity test, grip strength measurement, and motor activity measurement were performed once every 6 weeks after administration.

Female:

Detailed observation was conducted weekly during the administration and recovery periods. However, only the satellite group was observed for 6 weeks after administration.

Reactivity test, grip strength measurement, and motor activity measurement were performed on the day before anatomy in the parturition animals and once every 6 weeks in the satellite group.

BODY WEIGHT: Yes

- Time schedule for examinations:

Males, females (satellite):

On days 1, 8, 15, 22, 29, 36, and 42 of administration period. On days 1, 8 and 14 of recovery period.

Females (mating):

Before mating, measurements were taken on days 1, 8 and 15 of administration. Mated females were measured at gestation 0, 7, 14, and 20. The delivered females were measured on the day of delivery and 4 days after delivery.

FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):

- Food consumption: Yes

- Time schedule for examinations:

Males, females (satellite):

On days 1, 8, 15, 29, 36, 42 of administration period.

On days 1, 8, 14 of recovery period.

Females (mating):

On days 1, 8, 15 of administration period, on days 0, 7, 14, 20 of gestation period, on days 0, 4 of lactation period.

WATER INTAKE: No

OPHTHALMOSCOPIC EXAMINATION: No

HAEMATOLOGY: Yes

- Time schedule for collection of blood:

At the end of administration period, or at the end of recovery period in both sexes

- Anaesthetic used for blood collection: ether

- Animals fasted: Yes

- How many animals:

At the end of administration period:

Males: 7, 12, 12, and 7 males/dose (0, 20, 100, and 500 mg/kg bw/day)

Females (mating): 12 females/dose (0, 20, 100, and 500 mg/kg bw/day),

Females (satellite): 5 females/dose (0 and 500 mg/kg bw/day)

At the end of recovery period:

5 males/dose and 5 females (satellite)/dose (0 and 500 mg/kg bw/day)

- Parameters examined: red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, reticulocyte percentage, platelet count, white blood cell count, differential white blood cell count, prothrombin time, activated partial thromboplastin time.

CLINICAL BIOCHEMISTRY: Yes

- Time schedule for collection of blood:

At the end of administration period, or at the end of recovery period in both sexes

- Animals fasted: Yes

- How many animals:

At the end of administration period:

Males: 7, 12, 12, and 7 males/dose (0, 20, 100, and 500 mg/kg bw/day)

Females (mating): 12 females/dose (0, 20, 100, and 500 mg/kg bw/day),

Females (satellite): 5 females/dose (0 and 500 mg/kg bw/day)

At the end of recovery period:

5 males/dose and 5 females (satellite)/dose (0 and 500 mg/kg bw/day)

- Parameters checked: total protein, albumin, A/G ratio, total bilirubin, glucose, total cholesterol, triglyceride, phospholipid, AST, ALT, LDH, ALP, γ -GT, CK, BUN, creatinine, sodium, potassium, chloride, calcium, inorganic phosphorus

BLOOD HORMONE: Yes

- Time schedule for collection of serum:

At the end of administration period, or at the end of recovery period in both sexes

- Animals fasted: Yes

- How many animals:

At the end of administration period:

Males: 7, 12, 12, and 7 males/dose (0, 20, 100, and 500 mg/kg bw/day)

Females (mating): 12 females/dose (0, 20, 100, and 500 mg/kg bw/day),
Females (satellite): 5 females/dose (0 and 500 mg/kg bw/day)
At the end of recovery period:
5 males/dose and 5 females (satellite)/dose (0 and 500 mg/kg bw/day)
- Parameters checked: Triiodothyronine (T3), Thyroxin (T4), and thyroid stimulating hormone (TSH)

URINALYSIS: Yes

- Time schedule for collection of urine:
Male, female satellite group: Fresh urine was collected before administration once at week 6 of administration period.
- Metabolism cages used for collection of urine: No
A urine collector to collect fresh urine samples under ad libitum feeding and drinking conditions.
- How many animals:
At the end of administration period:
Male: 7, 12, 12, and 7 males/dose (0, 20, 100, and 500 mg/kg bw/day)
Females (satellite): 10 females/dose (0 and 500 mg/kg bw/day)
- Parameters checked:
Fresh urine: pH, protein, glucose, ketones, bilirubin, occult blood, urobilinogen

NEUROBEHAVIOURAL EXAMINATION: Yes

- Time schedule for examinations:
Males and females (satellite): Week 6 of administration period.
Females (mating): The animals were delivered on the day before dissection (4 days after delivery).
- Dose groups that were examined: Autopsy animals after the end of the administration period
- Battery of functions tested:
1) Reflex/reactions (Manipulative Test). Visual forelimb placing response, auditory reactivity, tail pinch response, pupillary reflex, aerial righting reaction.
2) Measurement of Grip Strength. Grip strength of forelimb and hind limb was measured by MK-380CM (Muromachi kikai Co.,Ltd.).
3) Measurement of Spontaneous Motor Activity. Spontaneous motor activity was measured by SCAN ET MV-10 (MELQUEST Ltd.).
Motor activity was measured for 60 min.

Oestrous cyclicity (parental animals)

Vaginal smears were collected from all females except satellites and microscopically examined every day from the day after the start of administration until the day copulation was confirmed.

Sperm parameters (parental animals)

Parameters examined in all P male parental generations: testes, epididymis ventral prostate, and seminal vesicle weight, histopathological examinations for testes, epididymis ventral prostate, and seminal vesicle.

Litter observations

PARAMETERS EXAMINED: The following parameters were examined in F1 offspring: Number and sex of pups, stillbirths, live births, postnatal mortality, presence of gross anomalies, and weight gain.
GROSS EXAMINATION OF DEAD PUPS: Yes, for external and internal abnormalities.

Postmortem examinations (parental animals)

METHOD OF SACRIFICED: All animals were sacrificed by exsanguination under ether anesthesia.
SACRIFICE: Males, females (satellite): On next day after the last administration, Maternal animals: on Day 5 of lactation, Females who copulated but did not deliver: The day corresponding to GD 26, Males and females recovery group: on Day 14 of recovery.

GROSS PATHOLOGY: Yes

ORGAN WEIGHT: Yes

: pituitary, thyroids, heart, liver, kidney, thymus, spleen, adrenal gland, testes, epididymides, ventral prostate, seminal vesicles (including coagulating gland) , ovaries, uterus, brain, lung

HISTOPATHOLOGY: Yes: brain. pituitary, spinal cord, eye ball, thyroid, parathyroid, heart, nasal cavity, trachea, lung, liver, kidney, thymus, spleen, adrenal glands, stomach, small intestine (including duodenum), large intestine, testis, epididymis, ventral prostate, seminal vesicles (including coagulating gland), ovaries, uterus, vagina, urinary bladder, lymph nodes (axillary, inguinal, etc.), peripheral nerve (sciatic nerve), bone marrows (femur), bone (femur), mammary gland, muscle.

Postmortem examinations (offspring)

SACRIFICE

- The F1 offsprings were euthanized on PND4 by exsanguination under ether anesthesia.

GROSS NECROPSY: Yes

- Gross necropsy consisted of external and internal examinations including the cervical, thoracic, and abdominal viscera.

HISTOPATHOLOGY / ORGAN WEIGHTS

- Not examined.

Statistics

For copulation index, fertility index, gestation index, urinalysis and histopathological findings, statistical difference between each treatment group and the control group was analyzed using by the Chi-square test.

For quantitative data, homogeneity of variance was tested using Bartlett method first. If the variance was homogenous, statistical difference between each treatment group and the control group was analyzed using Dunnett method. If not homogenous, statistical difference between each treatment group and the control group was tested using Kurskal-Wallis rank sum test and the significant difference between the medium control and treated groups was analyzed by nonparametric Dunnett multiple comparison test. For comparison of quantitative data between two groups in female satellite animals and male recovery test, homogeneity of variance was analyzed by F-test. Then, if homogenous, student's t-test was applied. If not homogenous, Aspin-Welch's t-test was used.

Reproductive indices

Each parameter was determined by the following equations:

Copulation index (%) = (No. of copulated pairs / No. of mated pairs) × 100

Fertility index (%) = (No. of pregnant females / No. of copulated pairs) × 100

Gestation index (%) = (No. of females with complete parturition / No. of pregnant females) × 100

Gestation length (days)

Implantation index (%) = (No. of implantations / No. of corpora lutea) × 100

Delivery index (%) = (No. of pups born / No. of implantation) × 100

Birth index (%) = (No. of live pups on day 0 / No. of implantation) × 100

Live birth index (%) = (No. of live pups on day 0 / No. of pups born) × 100

Sex ratio on pups born = No. of male pups / No. of male and female pups born

Sex ratio on day 4 = No. of male live pups on day 4 / No. of live pups on day 4

Offspring viability indices

Viability index (%) = (No. of live pups on day 4 / No. of live pups on day 0) × 100

Results and discussion

Results: P0 (first parental generation)

General toxicity (P0)

Clinical signs

effects observed, treatment-related

Description (incidence and severity)

See 7.5.1 Repeated dose toxicity. 001

Mortality

mortality observed, non-treatment-related

Description (incidence)

See 7.5.1 Repeated dose toxicity. 001

Body weight and weight changes

effects observed, treatment-related

Description (incidence and severity)

See 7.5.1 Repeated dose toxicity. 001

Food consumption and compound intake (if feeding study)

no effects observed

Food efficiency

not examined

Water consumption and compound intake (if drinking water study)

not examined

Ophthalmological findings

not examined

Haematological findings

not specified

Description (incidence and severity)

See 7.5.1

Clinical biochemistry findings

not specified

Description (incidence and severity)

See 7.5.1 Repeated dose toxicity. 001

Urinalysis findings

no effects observed

Behaviour (functional findings)

no effects observed

Immunological findings

not examined

Organ weight findings including organ / body weight ratios

no effects observed

Gross pathological findings

no effects observed

Neuropathological findings

not examined

Histopathological findings: non-neoplastic

no effects observed

Histopathological findings: neoplastic
not examined

Reproductive function / performance (P0)

Reproductive function: oestrous cycle
no effects observed

Reproductive function: sperm measures
no effects observed

Reproductive performance
no effects observed

Details on results (P0)

General toxicity: See 7.5.1 Repeated dose toxicity. 001

Reproductive function / performance: There were no effects on reproductive parameters up to 500 mg/kg bw/day.

Effect levels (P0)

Key result

true

Dose descriptor

NOAEL

Effect level

500

mg/kg bw/day (actual dose received)

Based on

test mat.

Sex

male/female

Basis for effect level

other: No effects on reproduction

Results: F1 generation

General toxicity (F1)

Clinical signs

no effects observed

Mortality / viability

no mortality observed

Body weight and weight changes

no effects observed

Gross pathological findings

no effects observed

Details on results (F1)

There were no effects on developmental parameters up to 500 mg/kg bw/day.

Effect levels (F1)

Key result

true

Dose descriptor

NOAEL

Generation

F1

Effect level

500

mg/kg bw/day (actual dose received)

Based on

test mat.

Sex

male/female

Basis for effect level

other: No effects on development

Overall reproductive toxicity

Key result

true

Reproductive effects observed

no

Any other information on results incl. tables

Figures and Tables (in English) are available in the following full report of the study.
https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF88-61-9d.pdf

Applicant's summary and conclusion

Conclusions

In the combined repeated oral dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) described above, there were no effects on reproductive and developmental parameters up to 500 mg/kg bw/day. The NOAEL for the rat reproductive/developmental toxicity of 2,4-Dimethylbenzenesulfonic acid was regarded as 500 mg/kg bw/day, the highest dose tested.

Executive summary

In the combined repeated dose and reproductive/developmental screening test (OECD TG422), SD rats were treated orally with the test substance at the doses of 0, 20, 100 and 500 mg/kg bw/day. Males were

dosed for 42 days including a 14 day pre-mating period. Females (12 animals/dose) were dosed for 41-46 days including 14 day pre-mating, mating, and gestation periods and days until day 4 of lactation. In addition, as the satellite study group of females (10 females/group) was dosed 0 and 500 mg/kg/day for 42 days, with 5 animals/group treated with recovery. There were no effects on reproductive and developmental parameters up to 500 mg/kg bw/day. The NOAEL for the rat reproductive/developmental toxicity of 2,4-dimethylbenzenesulfonic acid was regarded as 500 mg/kg bw/day, the highest dose tested.

References

Reference Substances

REFERENCE_SUBSTANCE: m-xylene-4-sulphonic acid

UUID: ECB5-25d98114-4c1a-4381-882e-fa63892577f7

Dossier UUID:

Author:

Date: 2007-05-10T18:00:00.000+09:00

Remarks:

Reference substance name

m-xylene-4-sulphonic acid

IUPAC name

2,4-dimethylbenzenesulfonic acid

Inventory

Inventory number

Inventory name

m-xylene-4-sulphonic acid

Inventory

EC Inventory

Inventory number

201-843-9

CAS number

88-61-9

Molecular formula

C₈H₁₀O₃S

Description

CAS number

88-61-9

Synonyms

Synonyms

Identity

Benzenesulfonic acid, 2,4-dimethyl-

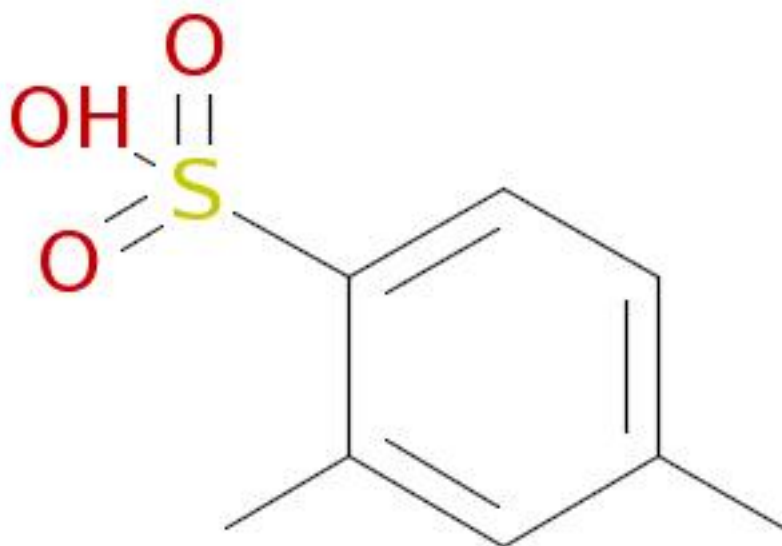
Identity

Benzenesulfonic acid, 2,4-dimethyl-

Molecular and structural information

Molecular formulaC₈H₁₀O₃S**Molecular weight**

186.2282

SMILES notationCc1ccc(c(C)c1)S(=O)(=O)O**InChI**InChI=1/C₈H₁₀O₃S/c1-6-3-4-8(7(2)5-6)12(9,10)11/h3-5H,1-2H3,(H,9,10,11)**Structural formula**

Related substances**Group / category information**

DSL Category: Organics

Test Materials

TEST_MATERIAL_INFORMATION: 2,4-Dimethylbenzenesulfonic acid

UUID: 889d6bfe-5432-4110-bc28-9bf04b35ad65

Dossier UUID:

Author:

Date: 2021-03-04T09:50:09.000+09:00

Remarks:

Name

2,4-Dimethylbenzenesulfonic acid

Literatures

LITERATURE: Combined repeated dose toxicity study with the reproductive/developmental toxicity screening test of 2,4-Dimethylbenzenesulfonic acid by oral administration in rats

UUID: 5c5e4887-b688-420d-a735-389d5aa77069

Dossier UUID:

Author:

Date: 2021-03-04T09:35:01.000+09:00

Remarks:

General information

Reference Type
study report

Title
Combined repeated dose toxicity study with the reproductive/developmental toxicity screening test of 2,4-Dimethylbenzenesulfonic acid by oral administration in rats

Author
Ministry of Health, Labour and Welfare (MHLW), Japan

Bibliographic source
available in the web of Japan Existing Chemical Data Base (JECDB)
https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF88-61-9d.pdf

Testing facility
Japan Bioassay Research Center

Report number
0765

LITERATURE: In Vitro Chromosomal Aberration Test of on 2,4-Dimethylbenzenesulfonic acid Cultured Chinese Hamster Cells.

UUID: 54541599-236b-4c5c-b2aa-7afdc5e9032

Dossier UUID:

Author:

Date: 2021-03-15T16:17:50.000+09:00

Remarks:

General information

Reference Type

study report

Title

In Vitro Chromosomal Aberration Test of on 2,4-Dimethylbenzenesulfonic acid Cultured Chinese Hamster Cells.

Author

Ministry of Health, Labour and Welfare (MHLW), Japan

Year

2011

Bibliographic source

Japan Existing Chemical Data Base (JECDB)

https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF88-61-9f.pdf

Testing facility

Japan Bioassay Research Center

Report number

7416

LITERATURE: Reverse Mutation Test of 2,4-Dimethylbenzenesulfonic acid on Bacteria.

UUID: 478e3901-a792-4655-941f-4bcb69910f50

Dossier UUID:

Author:

Date: 2021-03-10T15:31:49.000+09:00

Remarks:

General information

Reference Type

study report

Title

Reverse Mutation Test of 2,4-Dimethylbenzenesulfonic acid on Bacteria.

Author

Ministry of Health, Labour and Welfare (MHLW), Japan

Year

2011

Bibliographic source

Japan Existing Chemical Data Base (JECDB)

https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF88-61-9e.pdf

Testing facility

Japan Bioassay Research Center

Report number

6337

Legal Entities

LEGAL_ENTITY: National Institute of Health Sciences

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Dossier UUID:

Author:

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Remarks:

General information

Legal entity name

National Institute of Health Sciences

Remarks

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Identifiers

Other IT system identifiers

IT system
LEO
ID
10767
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ID

16558402024DIV750