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 Sciences

Printing date: 2022-11-29T15:15:35.007+09:00

Table of Contents

DOSSIER:

UUID: 0
Dossier UUID:
Author:
Date: 2022-11-29T15:15:34.882+09:00
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

UUID:	f51e7b54-9211-4863-90ce-fcf8a155d647
Dossier UUID:	
Author:	
Date:	2022-11-07T16:24:02.822+09:00
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	EC name
201-843-9	EC Inventory
CAS number	**CAS name**
88-61-9	

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 equipmen t 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 remaind er.

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. Ana lytical 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 gr oup 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 (Crl: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 l actation 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, mea n corpuscular hemoglobin, mean corpuscular hemoglobin concentration, reticulocyte percentage, platelet count, white blood cell count, differential white blood cell count, prothrombin time, activated p artial 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, trigly ceride, phospholipid, AST, ALT, LDH, ALP, γ-GT, CK, BUN, creatinine, sodium, potassium, chloride, ca lcium, 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 duo denum), 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 copulation index, fertility index, gestation index, urinalysis and histopathological findings, s tatistical difference between each treatment group and the control group was analyzed using by the C hi-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 g roup and the control group was tested using Kurskal-Wallis rank sum test and the significant differe nce 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 animales/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

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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 ug/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-amimoacridine 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 i ncrease was observed.

Statistics
no

Results and discussion

Test results

Key result
true

Species / strain
S. 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 / strain
S. 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

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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

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

Deviations
no

GLP compliance
yes

Type of assay
in 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(±): 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 Japanease) 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 equipmen t 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 remaind er.

Test animals

Species
rat

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 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. Ana lytical 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 gr oup 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 (Crl: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 l actation 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, mea n corpuscular hemoglobin, mean corpuscular hemoglobin concentration, reticulocyte percentage, platelet count, white blood cell count, differential white blood cell count, prothrombin time, activated p artial 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, tri glyceride, 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 sem inal vesicle weight, histopathological examinations for testes, epididymis ventral prostate, and sem inal 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 WEIGTHS
- 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 scree ning 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 formula
C8H10O3S

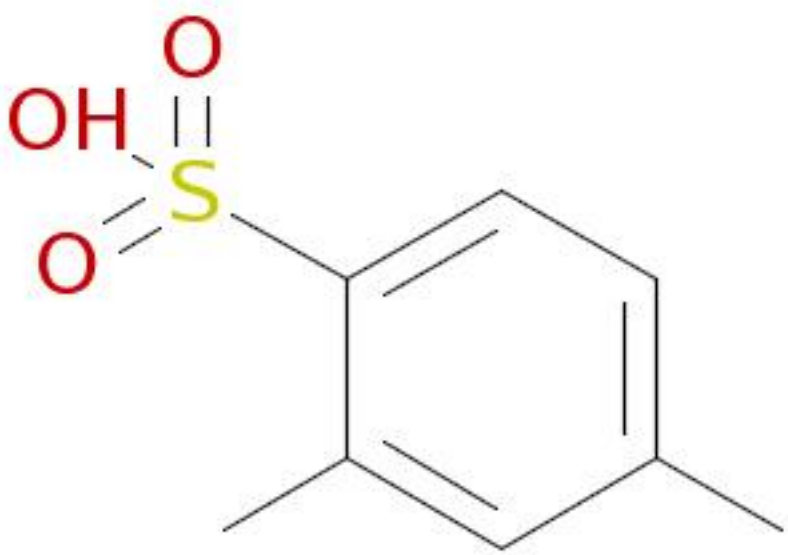
Molecular weight

186.2282

SMILES notation
Cc1ccc(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-7afdcd5e9032
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

UUID: IUC4-b036ff75-0f3c-323b-b200-ed5f46cf5101
Dossier UUID:
Author:
Date: 2022-11-07T15:49:29.000+09:00
Remarks:

General information

Legal entity name
National Institute of Health Sciences

Remarks
Disclaimer: The contents in this document were created based on the MHLW (Ministry of Health, Labour and Welfare) peer reviewed study reports (in Japanese) in JECDB (Japan Existing Chemical Database) at http://dra4.nihs.go.jp/mhlw_data/jsp/SearchPageENG.jsp. Authorship is in the Division of Risk Assessment, the National Institute of Health Sciences, and the contents do not reflect any o fficial MHLW opinions or any other regulatory policies.

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Town
Kawasaki

Region / State
Kanagawa

Country
Japan
JP

Identifiers

Other IT system identifiers

IT system LEO **ID** 10767
IT system IUCLID4

ID
16558402024DIV750