Name: 4-chloro-m-cresol / 59-50-7

Legal entity owner: National Institute of Health Sciences / Kawasaki / Japan

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4-chloro-m-cresol

CORE

General information

Identification

SUBSTANCE: 4-chloro-m-cresol

UUID: 053ede1d-07b6-42db-ba58-88a6a246d151
Dossier UUID:
Author: SuperUser
Date: 2019-09-03T09:59:28.332+09:00
Remarks:

Substance name
4-chloro-m-cresol

Other identifiers

Identifier
CAS number

Identity
59-50-7

Legal entity
National Institute of Health Sciences / Kawasaki / Japan

Identification of substance

Reference substance
4-chloro-m-cresol / 59-50-7

EC number	EC name
CAS number	CAS name
59-50-7	
IUPAC name	

Role in the supply chain

Manufacturer
false

Importer
false

Only representative
false

Downstream user
false

OECD

Health Effects

Repeated dose toxicity: oral

ENDPOINT_STUDY_RECORD: Repeated dose toxicity: oral.002

UUID: e6fae949-411a-4c4b-96ab-8f8ac06d87f2
Dossier UUID:
Author: Dra
Date: 2018-03-30T09:01:58.619+09:00
Remarks:

Administrative data

Endpoint
repeated dose toxicity: oral, other screening for reproductive / developmental toxicity

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
Reliability 1

Cross-reference

Reason / purpose
reference to same study

Related information
OECD / Toxicity to reproduction / Toxicity to reproduction.001 / 4-chloro-m-cresol / 59-50-7

Data source

Reference

A reproduction/developmental toxicity screening test in rats treated orally with 4-chloro-m-cresol / Ministry of Health, Labor and Welfare, Japan / study report

Data access
data published

Materials and methods

Test guideline

Qualifier
according to

Guideline
other: OECD Guideline 421 (Reproduction / Developmental Toxicity Screening Test)

Deviations
no

GLP compliance
yes

Limit test
no

Test material

Specific details on test material used for the study
- Analytical purity: 99.9%
- Storage condition of test material: at a cold (temperature 1-8 °C) and dark place, with airtight s topper.
- 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 and environmental conditions
TEST ANIMALS
- Source: Charle s River Japan, Inc., Atsugi Breeding Center.
- Age at study initiation: 10 weeks old
- Weight at study initiation: Male: 398.6 g (366 -432 g), Female: 257.2 g (235-283 g)
- Housing: Animals were housed individually, except for during the acclimation (two animals by sex), mating (one male and one female) and lactation periods (one litter), in metallic bracket-type cages with wire mesh floors (260W x 380D x 180H mm). From gestation day 17 to lactation day 4, individual dams and litters were reared on bedding.
- Diet: Solid feed (CRF-1: Oriental Yeast Co., ltd.) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation period: 14 days
ENVIRONMENTAL CONDITIONS
- Temperature (°C): 22±3 (actual temperature: 21-25°C)
- Humidity (%): 50±20% (actual humidity: 36-62%)

- Air changes (per hr): 10-15
- Photoperiod (hrs dark / hrs light): 12 hr dark/12 hr light (light: 8:00~20:00)

Administration / exposure

Route of administration
oral: gavage

Vehicle
corn oil

Details on oral 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 or sperm in vaginal smear referred to as day 0 of pregnancy
- After 14 days of unsuccessful pairing replacement of first male by another male with proven fertility.

Analytical verification of doses or concentrations
yes

Duration of treatment / exposure
(P) Males: 42 days including 14 days pre-mating and mating periods, and thereafter 14 days
(P) Females: up to 56 days including 14 days pre-mating, mating and gestation periods, and the days until day 3 of lactation

Frequency of treatment
Once/day, 7days/week

Doses / concentrations

Dose / conc.	
0	mg/kg bw/day (actual dose received)
Dose / conc.	
35	mg/kg bw/day (actual dose received)
Dose / conc.	
150	mg/kg bw/day (actual dose received)
Dose / conc.	
600	mg/kg bw/day (actual dose received)

No. of animals per sex per dose
12 animals/sex/dose

Control animals
yes, concurrent vehicle

Details on study design
- Dose selection rationale: Based on the results of a 14-day preliminary study, the highest dose of 600 mg/kg bw/day was selected as an expected obvious toxic dose, and the lowest dose of 35 mg/kg bw /day was selected as an expected no toxic dose. The middle dose levels of 150 mg/kg bw/day were selected.
- Rationale for animal assignment (if not random): Body weight-balanced randomization

[14-day preliminary study]
A 14-day repeated dose oral toxicity test (Crl:CD(SD) rats, doses: 0 (olive oil), 35, 150, and 600 mg/kg bw/day). At 600 mg/kg bw/day, staggering gait, soiled perineal region, yellowish white mass in the cauda epididymis were observed.

Examinations

Observations and examinations performed and frequency
CAGE SIDE OBSERVATIONS: Yes
- Time schedule: Males and females: 2 times/day

DETAILED CLINICAL OBSERVATIONS: No

BODY WEIGHT: Yes
- Time schedule for examinations:
Males: Days 1, 2, 5, 7, 10, 14, 21, 28, 35, 42, and the day of necropsy
Females: Days 1, 2, 5, 7, 10, and 14; gestation days 0, 1, 3, 5, 7, 10, 14, 17, and 20; lactation days 0, 1 and 4; and the day of necropsy. For unmating females, 21 and 28 in the mating period
FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):
- Food consumption: Yes
Males: Days 1, 2, 5, 7, 10, 14, 21, 28, 35, and 42, in dosing period
Females: Days 1, 2, 5, 7, 10, and 14; gestation days 0, 1, 3, 5, 7, 10, 14, 17, and 20; lactation days 0, 1 and 4
OTHER: Females: Numbers of corpus luteum and implantation site on the day of necropsy

Sacrifice and pathology
SACRIFICE
- Male animals: All surviving animals were euthanized by exsanguination under ether anesthesia on the day after the last administration.
- Maternal animals: All surviving animals were euthanized by exsanguination under ether anesthesia on day 4 of lactation.

GROSS NECROPSY: Yes (gross necropsy consisted of external and internal examinations including the cervical, thoracic, and abdominal viscera.)

HISTOPATHOLOGY: Yes (Male: testis, epididymis, and gross abnormal site (ileum); Female: ovary, and gross abnormal site (pituitary gland, thymus, spleen, kidney, ileum))

Other examinations
ORGAN WEIGHTS: Yes (brain, thymus, heart, liver, kidney, spleen, adrenal, testis, epididymis, ovary)

Statistics
Body weights, body weight gain, food consumption, organ weights and relative organ weights, stages of spermatogenesis, length of the estrous cycle, number of corpora lutea, number of implantation sites, implantation index, delivery index, number of pups delivered, number of live pups, live birth index, sex ratio, number of live pups and viability index at lactation day4 were analyzed for statistical significance in the following way: homogeneity of variance was evaluated first by Bartlett's test. When group variances were homogeneous, the one-way analysis of variance was used to determine if any statistical differences existed among the groups. If the analysis of variance gave a significant result, Dunnett's test was performed to detect any significant differences between the treated groups and their corresponding controls. When Bartlett's test indicated that the variances were not homoge

neous, the Kruskal-Wallis test was used for detecting any statistical differences and if they were significant, the Mann-Whitney U test was performed to detect any significant differences between th e treated groups and their corresponding controls. The incidences of females with abnormal estrous cyclicity, and indices of copulation, fertility and gestation, and nursing index were analyzed by the Chi-square test or Fisher's exact probability test.

Results and discussion

Results of examinations

Clinical signs
effects observed, treatment-related

Description (incidence and severity)
Decrease in locomotor activity was observed in one male on day 5 and 6, in one female on day 1 at 600 mg/kg bw/kg.
Crawling position, lateral position and soil of perigenital fur were observed in males and females at 600 mg/kg bw/kg.

Mortality
no mortality observed

Body weight and weight changes
effects observed, treatment-related

Description (incidence and severity)
Significantly low value of body weight was observed in both sexes at 600 mg/kg bw/day.

Food consumption and compound intake (if feeding study)
effects observed, treatment-related

Description (incidence and severity)
Significantly low value of food consumption was observed in both sexes at 600 mg/kg bw/day.

Food efficiency
not examined

Water consumption and compound intake (if drinking water study)
not examined

Ophthalmological findings
not examined

Haematological findings
not examined

Clinical biochemistry findings
not examined

Urinalysis findings
not examined

Behaviour (functional findings)
not examined

Immunological findings
not examined

Organ weight findings including organ / body weight ratios
effects observed, treatment-related

Description (incidence and severity)
[treatment-related effect]:
Increases in relative kidney weight was observed in both sexes at 600 mg/kg bw/day.

[non-treatment-related]:
Increases in relative brain weight was observed in both sexes at 600 mg/kg bw/day.
However, this change was considered due to the reduction in terminal body weights. Therefore this change was no toxicological meaning.

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

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

Based on
test mat.

Sex
male/female

Basis for effect level
clinical signs
Decrease in locomotor activity was observed in one male on day 5 and 6, in one female on day 1 at 600 mg/kg bw/kg. Crawling position, lateral position and soil of perigenital fur were observed in males and females at 600 mg/kg bw/kg.
body weight and weight gain
Significantly low value of body weight was observed in both sexes at 600 mg/kg bw/day.
food consumption and compound intake
Significantly low value of food consumption was observed in both sexes at 600 mg/kg bw/day.

Any other information on results incl. tables

Figures and Tables (in English) are available in the following full report of the study.

http://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF59-50-7c.pdf

Applicant's summary and conclusion

Executive summary

A reproduction/developmental toxicity screening test was performed according to OECD TG 421. Male and female rats (12 animals/sex/dose) were administered 4 -chloro-m-cresol at 0, 35, 150, and 600 mg/kg bw/day. Males were dosed for 42 days, including a 14 day pre-mating and mating periods. Females were dosed for 56 days, including a 14 day pre-mating, mating, and gestation periods, and the time until lactation day 3. Decrease in locomotor activity was observed in both sexes at 600 mg/kg bw/kg. Crawling position, lateral position and soil of perigenital fur were observed in both sexes at 600 mg/kg bw/kg. Significantly low value of body weight was observed in both sexes at 600 mg/kg bw/day. Significantly low value of food consumption was observed in both sexes at 600 mg/kg bw/day. On the basis of these effects, NOAEL for repeated-dose toxicity was determined to be 150 mg/kg bw/day in male and female rats.

ENDPOINT_STUDY_RECORD: Repeated dose toxicity: oral.001

UUID: 71fc6c21-ce5b-44d5-acd3-ac5a76818149
Dossier UUID:
Author: Dra
Date: 2018-03-30T09:01:58.681+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
true

Used for classification
true

Used for SDS
false

Study period
28 days

Reliability
1 (reliable without restriction)

Rationale for reliability incl. deficiencies
guideline study
Reliability 1

Data source

Reference

Twenty-eight-day Repeat Dose Oral Toxicity Test of 4-chloro-m-cresol in Rats / Ministry of Health, Labor and Welfare, Japan / study report

Data access
data published

Materials and methods

Test guideline

Qualifier
according to

Guideline
other: Guideline for 28-Day Repeated Dose Toxicity Test in Mammalian Species (Chemical Subs tances Control Law of Japan)

Qualifier
equivalent or similar to

Guideline
OECD Guideline 407 (Repeated Dose 28-Day Oral Toxicity in Rodents)

GLP compliance
yes

Limit test
no

Test material

Specific details on test material used for the study
- Name of test material (as cited in study report): 4-chloro-m-cresol
- Purity: 99.9%
- Storage condition of test material: at a cold (temperature 2-6°C) and dark place, with airtight stopper.
- Stability under test conditions: stable
- Solubility and stability of the test substance in the solvent/vehicle: stable

Test animals

Species
rat
common rodent species

Strain
other: Crl:CD(SD)

Sex
male/female

Details on test animals and environmental conditions
TEST ANIMALS
- Source: Charles River Laboratories Japan Inc., Atsugi Breeding Center.
- Age at study initiation: 5 weeks old
- Weight at study initiation: male 160g (145-171g), female 142g (130-153g)
- Housing: Animals were individually housed in stainless wire-meshed cages (260W × 380D × 180H mm).
- Diet: Solid feed (MR stock: Nosan Corporation) was given ad libitum.
- Water: irradiated tap water, ad libitum.
- Acclimation period: 7-8 days

ENVIRONMENTAL CONDITIONS
- Temperature (°C): 22±3°C (actual temperature: 21.5-22.1°C)
- Humidity (%): 55±10% (actual humidity: 53-60%)
- Air changes (per hr): more than ten times per hr
- Photoperiod (hrs dark / hrs light): 12 hrs dark / 12 hrs light (light: 7:00-19:00)

Administration / exposure

Route of administration
oral: gavage

Vehicle
olive oil

Details on oral exposure
- Amount of vehicle (if gavage): 5 mL/kg
- Dosing volume: 5 mL/kg

Analytical verification of doses or concentrations
yes

Duration of treatment / exposure
28 days

Frequency of treatment
Once/day, 7 days/week

Doses / concentrations

Dose / conc.	
0	mg/kg bw/day (actual dose received)
Dose / conc.	
15	mg/kg bw/day (actual dose received)
Dose / conc.	
60	mg/kg bw/day (actual dose received)
Dose / conc.	
250	mg/kg bw/day (actual dose received)
Dose / conc.	
1000	mg/kg bw/day (actual dose received)

No. of animals per sex per dose
Control and high-dose group: 10 animals/sex/ (including recovery group of 5 animals/sex/each group)
Low- and middle-dose group: 5 animals/sex/dose

Control animals
yes, concurrent vehicle

Details on study design
- Dose selection rationale: Based on the results of a 14-day preliminary study, the highest dose of 1000 mg/kg bw/day was selected as an expected obvious toxic dose, and the lowest dose of 15 mg/kg bw/day was selected as an expected no toxic dose. The middle dose levels of 60 and 250mg/kg bw/day were selected.

- Rationale for animal assignment (if not random): Body weight-balanced randomization
- Rationale for selecting satellite groups: Reversibility of toxic effects by treatment was examined in recovery test with control- and high-dose groups for both sexes.
- Post-exposure recovery period in satellite groups: 14 days

[14-day preliminary study]
A 14-day repeated dose oral toxicity test (Crl:CD(SD) rats, doses: 0 (olive oil), 50, 150, 100, 500 or 1000 mg/kg bw/day). At 500 mg/kg bw/day or more or 1000 mg/kg bw/day, tremor, decrease in locomotor activity, prone position and salivation, depression body weight gain, tendency of low food consumption, decrease in platelet, total bilirubin, cholinesterase and urine protein, increase in total cholesterol and potassium were observed. At 1000 mg/kg bw/day, increase in relative brain weight, decrease in absolute spleen weight, and slight thickening of forestomach were observed.

Examinations

Observations and examinations performed and frequency
CAGE SIDE OBSERVATIONS: Yes
- Time schedule: every day during the administration (4 times a day) and recovery periods (at least once a day)

DETAILED CLINICAL OBSERVATIONS: Yes
- Time schedule: Once before the start of administration, and once every week by the end of the study period.

BODY WEIGHT: Yes
- Time schedule for examinations: Before administration (on days 1, 7, 14, 21 and 28 of the administration period, days 7 and 14 of the recovery period) and the necropsy days after completion of every period.

FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):
- Food consumption: Yes. Once a week for 24-h (males: on days 5, 12, 19 and 26 of the administration period and days 5 and 12 of the recovery period.
females: on days 4, 11, 18 and 25 of the administration period and days 4 and 11 of the recovery period)

OPHTHALMOSCOPIC EXAMINATION: No

HAEMATOLOGY: Yes
- Time schedule for collection of blood: the day after completion of the administration and recovery periods
- Anaesthetic used for blood collection: ether
- Animals fasted: Yes(overnight)
- How many animals: all animals
- Parameters examined included RBC, hemoglobin, hematocrit, MCV, MCH, MCHC, platelet, reticulocyte, PT, APTT, WBC and differential WBC.

CLINICAL CHEMISTRY: Yes
- Time schedule for collection of blood: the day after completion of the administration and recovery periods
- Animals fasted: Yes(overnight)
- How many animals: all animals
- Parameters examined included total protein, albumin, A/G ratio, total bilirubin, glucose, total cholesterol, triglyceride, phospholipid, AST, ALT, LDH, ALP, gamma-GTP, BUN, creatinine, Na, K, Cl, Ca and IP.

URINALYSIS: Yes
- Time schedule for collection of urine: On weeks 4 of the administration period and weeks 2 of the recovery period.
- Metabolism cages used for collection of urine: Yes

- How many animals: All animals
- Parameters examined included color, cloudy, urine volume, specific gravity, Na, K, pH, protein, gl ucose, ketone body, bilirubin, occult blood and urobilinogen.

NEUROBEHAVIOURAL EXAMINATION: Yes
- Time schedule for examinations: Sensory motor reflexes, forelimb and hindlimb grip strengths, and motor activity were measured on week 4 of administration period (main/recovery group animals) and week 2 of recovery period (recovery group animals).
- Dose groups that were examined: All animals
- Battery of functions tested: sensory activity (hearing reaction, eye sight reaction, sense of touch reaction, pain reaction, pupil reflex, righting reflex), grip strength, motor activity

Sacrifice and pathology
GROSS PATHOLOGY: Yes

ORGAN WEIBHT: Yes [brain, pituitary gland, thyroid, adrenal, spleen, heart, liver, kidney, thymus, testis, epididymis, ovary]

HISTOPATHOLOGY: Yes [brain (cerebrum, cerebellum and medulla oblongata), pituitary gland, spina l cord (cervical, thoracical, lumber), thymus, thyroid (including parathyroid), adrenal glands, spleen, heart, stomach, liver, duodenum, jejunum, ileum (including Peyer's patches), cecum, colon, rectal, mesenteric lymph nodes, submandibular lymph nodes, trachea, lung, kidney, bladder, testis, epi didymis, prostate, seminal vesicles, ovary, uterus, vagina, eye, bone marrow (femur) and the sciatic nerve. (see tables in the study report.)]

Statistics
As for parametric data (grip strength, locomotor activity, body weight, body weight gain, food consu mption, hematology and clinical chemistry data, organ weights, quantitative urinalysis data), the v alues of means and standard deviations were calculated per group. When more than three groups exist in the test group, Bartlett test for variance was done, and if the variance was homogenous, ANOVA was applied. If the variance was not homogenous or data was non-parametric (differential W BC percentage, qualitative urinalysis data), Kruskal-Wallis rank sum test was used. Consequently, if the result was significant, Dunnett multiple comparison or Dunnett typed method was used for dete ction of statistical significance against control group. When the number of the test group was two, F-test was used as for parametric data.
Then, student's t-test or Aspin-Welch's t-test was applied depending on the result of homogeneity of variance. While, as for non-parametric data, Man-Whitney's U-test was applied. Furthermore, as for categorized data (incidence of abnormal findings in clinical observation, detailed observation, senso ry functional examination, necropsy and histopathology), Fischer's exact test was used. In any tests, level of significance was set at 5%.

Results and discussion

Results of examinations

Clinical signs
effects observed, treatment-related

Description (incidence and severity)
[treatment-related effect]:
Tremor, decrease in locomotor activity, ptosis, prone/side position, soiled perineal region and sal ivation were observed in one dead female at 1000 mg/kg bw/day.
Tremor, decrease in locomotor activity, ptosis, prone position were observed in all males and females at 1000 mg/kg bw/day.
Soiled perineal region was observed in all females at 1000 mg/kg bw/day.
Transient prone position in three males and decreased locomotor activity in two males were observed at 250 mg/kg bw/day.

[non-treatment-related effect]:
Transient salivation was observed in all males and females at 250 mg/kg bw/day or more. This finding was thought to be due to the irritancy of the test substance.

Mortality
mortality observed, treatment-related

Description (incidence)
One female animal died in the 1000 mg/kg bw/day.

Body weight and weight changes
effects observed, treatment-related

Description (incidence and severity)
Decreased body weight and depression of body weight gains were observed in the males at 1000 mg/kg bw.

Food consumption and compound intake (if feeding study)
effects observed, treatment-related

Description (incidence and severity)
Significant decrease in food consumption were observed in the males at 1000 mg/kg bw/day.

Food efficiency
not examined

Water consumption and compound intake (if drinking water study)
not examined

Ophthalmological findings
not examined

Haematological findings
effects observed, non-treatment-related

Description (incidence and severity)
Significant decrease in monocyte ratio in differentiation of leukocyte were observed in the females at 1000 mg/kg bw/day. These variations were within ranges of historical control data. Therefore, these changes were considered to be incidental and not to be related to treatment of the test substance.
Significant lower hematocrit and significant higher reticulocytes were observed in the males, significant higher RBC were observed in the females at 1000 mg/kg bw/day. These variations were within ranges of historical control data. Therefore, these changes were considered to be incidental and not to be related to treatment of the test substance.

Clinical biochemistry findings
effects observed, treatment-related

Description (incidence and severity)
[treatment-related effect]:
Significant increase in ALT levels were observed in the females at 1000 mg/kg bw.
[non-treatment-related effect]:
Significant lower total bilirubin were observed in the males at 1000 mg/kg bw/day. These variations were within ranges of historical control data. Therefore, these changes were considered to be incidental and not to be related to treatment of the test substance.
Significant higher total bilirubin were observed in the females at 1000 mg/kg bw/day. These variations were within ranges of historical control data. In addition, there were no other related changes. Therefore, these changes were considered to be incidental and not to be related to treatment of the test substance.

Urinalysis findings
no effects observed

Behaviour (functional findings)
no effects observed

Immunological findings
not examined

Organ weight findings including organ / body weight ratios
effects observed, treatment-related

Description (incidence and severity)
At the end of the dosing period, an increase in relative liver weight was observed in males and fema les at 1000 mg/kg bw/day.

Gross pathological findings
effects observed, treatment-related

Description (incidence and severity)
[treatment-related effect]:
At the end of the dosing period, slight thickening of forestomach mucosa was observed in all males at 1000 mg/kg bw/day.

[non-treatment-related effect]:
At the end of the recovery period, small testis (right side) was observed in one male at 1000 mg/kg bw/day. However, it was only one case, and it was known as a spontaneous lesion of rat. Therefore, this change was considered to be incidental and not to be related to treatment of the test substance.

Neuropathological findings
not examined

Histopathological findings: non-neoplastic
effects observed, treatment-related

Description (incidence and severity)
[treatment-related effect]:
Liver: Slight hypertrophy of centrilobular hepatocyte was observed in two male and three females at 1000 mg/kg bw/day.
Forestomach: Slight hyperplasia of squamous was observed in one male and two females at 250 mg/kg bw/day. Moderate hyperplasia of squamous was observed in all males at 1000 mg/kg bw/day. Slight and Moderate hyperplasia of squamous was observed in females at 1000 mg/kg bw/day. In one dead female at 1000 mg/kg bw/day, there were severe hyperplasia of squamous in fore stomach, slight congestive edema and inflammation in lung, slight hemorrhage in thymus and slight a trophy in spleen.
[non-treatment-related effect]:
Hematoidin crystal of lung, myocardial degeneration/fibrosis of heart were observed in males at 1000 mg/kg bw/day. Atrophy cortex of thymus was observed in females at 1000 mg/kg bw/day. However, these findings were only for each group, and these were known as a spontaneous lesion of rat. Th erefore, these changes were considered to be incidental and not to be related to treatment of the test substance.
Atrophy seminiferous tuble of testis (unilateral) was observed in one male at 1000 mg/kg bw/day. However, it was only one case, and it was known as a spontaneous lesion of rat. Therefore, this change was considered to be incidental and not to be related to treatment of the test substance.

Histopathological findings: neoplastic
not examined

Effect levels

Key result
false

Dose descriptor
NOAEL

Effect level

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

Based on
test mat.

Sex
male/female

Basis for effect level
organ weights and organ / body weight ratios
At the end of the dosing period, an increase in relative liver weight was observed in males and f emales at 1000 mg/kg bw/day.
gross pathology
At the end of the dosing period, slight thickening of forestomach mucosa was observed in all males at 1000 mg/kg bw/day.
histopathology: non-neoplastic
Liver: Slight hypertrophy of centrilobular hepatocyte was observed in two male and three females at 1000 mg/kg bw/day. Forestomach: Slight hyperplasia of squamous was observed in one male and two females at 250 mg/kg bw/day. Moderate hyperplasia of squamous was observed in all males and females at 1000 mg/kg bw/day.
other: In one dead female at 1000 mg/kg bw/day, there were severe hyperplasia of squamous in forestomach, slight congestive edema and inflammation in lung, slight hemorrhage in thymus and sl ight atrophy in spleen.

Any other information on results incl. tables

Figures and Tables (in English) are available in the following full report of the study.

http://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF59-50-7b.pdf

Applicant's summary and conclusion

Executive summary

A 28-day repeated-dose toxicity test was performed according to the Japanese guideline (similar to OECD TG 407). Male and female rats (5 animals/sex/dose) were administered 4-nitro-m-cresol at 0, 15, 60, 250, and 1,000 mg/kg bw/day. In addition, both sexes (5 animals/sex/dose) were administered 0 and 1,000 mg/kg bw/day of this substance for 28 days and examined after a 14-day recovery period.

At 1000 mg/kg bw/day, one female died during the administration period. Clinical observation revealed, decrease in locomotor activity and prone position were observed in males at 250 mg/kg bw/day, tremor, decrease in locomotor activity, prone/side position in both sexes at 1000 mg/kg bw/day. Soiled perineal region were also observed in females at 1000 mg/kg bw/day. Body weights, body weight gain and food consumption were decreased in males at 1000 mg/kg bw/day. Blood chemical examination revealed a high values for ALT activity in females at 1000 mg/kg bw/day. Relative liver weights were higher in males and females at 1000 mg/kg bw/day. Gross pathology revealed slight thickening of forestomach mucosa in males at 1000 mg/kg bw/day. Histopathological examination revealed hypertrophy of centrilobular hepatocyte in the liver in male and females at 1000 mg/kg bw/day, hyperplasia of squamous in the forestomach in both sexes at 250 mg/kg bw/dayor more.

On the basis of these effects, NOAEL for repeated-dose toxicity was determined to be 60 mg/kg bw/day in male and female rats.

Genetic toxicity in vitro

ENDPOINT_STUDY_RECORD: Genetic toxicity in vitro.001

UUID: 764bbe55-ffa6-468b-b592-12facb8c9342
Dossier UUID:
Author: SuperUser
Date: 2019-09-03T10:33:36.740+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
true

Used for classification
false

Used for SDS
false

Reliability
1 (reliable without restriction)

Rationale for reliability incl. deficiencies
guideline study
Reliability 1

Data source

Reference

Reverse Mutation Test of 4-chloro-m-cresol on Bacteria / MHLW (Ministry of Health, Labour and Welfare), Japan / study report

Data access
data published

Materials and methods

Test guideline

Qualifier
according to

Guideline
OECD Guideline 471 (Bacterial Reverse Mutation Assay)

in vitro gene mutation study in bacteria

Qualifier
according to

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

GLP compliance
yes

Type of assay
bacterial reverse mutation assay
in vitro gene mutation study in bacteria

Test material

Specific details on test material used for the study
- Name of test material (as cited in study report): 4-chloro-m-cresol
- CAS No.: 59-50-7
Lot No.: ASL1407
- Purity: 100%
- Supplier: Wako Pure Chemical Industries, Ltd.
- Boiling point : 235°C
- Melting point/Freezing point: 65.7°C
- Vapor pressure: 0.05 mmHg (20°C)
- Solubility: 1 g/260 mL (20°C) in water.
- Physical state: white powder
- Storage condition of test material: stored at room temperature (21.1-25.3°C), light shielding

Method

Species / strain

Species / strain
S. typhimurium TA 1535, TA 1537, TA 98, TA 100 and E. coli WP2
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
Preliminary study
+/-S9 mix:1.22, 4.88, 19.5, 78.1, 313, 1250, 5000 µg/plate
(growth inhibition was observed at >=313µg/plate in TA100 and TA1535 and at >=1250µg/plate in WP2uvrA/pKM101, TA98, and TA1537)

Main study
+/-S9 mix: 9.77, 19.5, 39.1, 78.1, 156, 313, 625 µg/plate (TA100, TA1535 strains)
+/-S9 mix: 19.5, 39.1, 78.1, 156, 313, 625, 1250 µg/plate (WP2uvrA/pKM101, TA98, TA1537 strains)

Vehicle
- Vehicle(s)/solvent(s) used: DMSO

Controls

Solvent controls
yes

Positive controls
yes

Positive control substance
9-aminoacridine
  9-aminoacridine hydrochloride, -S9mix: (TA1537)
sodium azide
  -S9 mix: (TA1535)
other: 2-(2-Furyl)-3-(5-nitro-2-furyl) acrylamide
  -S9mix: (TA 100, TA98 and WP2 uvrA/pKM101)

Remarks
-S9mix

Solvent controls
yes

Positive controls
yes

Positive control substance
other: 2-aminoanthracene
  (all strains)

Remarks
+S9 mix

Details on test system and conditions
METHOD OF APPLICATION: Preincubation
DURATION- Preincubation period: 20 min at 37°C
 - Exposure duration: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
not used

Results and discussion

Test results

Key result
false

Species / strain
S. typhimurium TA 100
bacteria

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity
yes +/-S9: at =>313 µg/plate

Vehicle controls valid
yes

Positive controls valid
yes

Key result
false

Species / strain
S. typhimurium TA 1535
bacteria

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity
yes +/-S9: at =>313 µg/plate

Vehicle controls valid
yes

Positive controls valid
yes

Key result
false

Species / strain
E. coli WP2 uvr A pKM 101
bacteria

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity
yes -S9mix: at=>625 µg/plate, +S9mix: at 1250 µg/plate

Vehicle controls valid
yes

Positive controls valid
yes

Key result
false

Species / strain
S. typhimurium TA 98
bacteria

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity
yes +/-S9mix: at =>625 µg/plate

Vehicle controls valid
yes

Positive controls valid
yes

Key result
false

Species / strain
S. typhimurium TA 1537
bacteria

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity
yes +/-S9mix: at =>625 µg/plate

Vehicle controls valid
yes

Positive controls valid
yes

Any other information on results incl. tables

Figures and Tables (in Japanese) are available in the following full report of the study. http://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF59-50-7e.pdf

Tables (in English) are attachted to this document. Please download the export file to see the Tables.

Applicant's summary and conclusion

Conclusions
In a bacterial reverse mutation assay using Salmonella typhimurium TA100, TA1535, TA98, and TA1537, and Escherichia coli WP2uvrA/pKM101 (OECD TG 471), 4-chloro-m-cresol was negative with or without metabolic activation.

ENDPOINT_STUDY_RECORD: Genetic toxicity in vitro.002

UUID: 126966d5-1d1f-48a0-8437-c0fb2b9ac1e2
Dossier UUID:
Author: SuperUser
Date: 2019-09-03T10:33:19.869+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
true

Used for classification
false

Used for SDS
false

Reliability
1 (reliable without restriction)

Rationale for reliability incl. deficiencies
guideline study
Reliability 1

Data source

Reference

In Vitro Chromosomal Aberration Test of 4-chloro-m-cresol on Cultured Chinese Hamster Cells / MHLW (Ministry of Health, Labour and Welfare), Japan / study report

Materials and methods

Test guideline

Qualifier
according to

Guideline
OECD Guideline 473 (In Vitro Mammalian Chromosome Aberration Test)
in vitro cytogenicity / chromosome aberration study in mammalian cells

Qualifier
according to

Guideline
JAPAN: Guidelines for Screening Mutagenicity Testing Of Chemicals

genetic toxicity in vitro, other

GLP compliance
yes

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

Test material

Specific details on test material used for the study
- Name of test material (as cited in study report): 4-chloro-m-cresol
- CAS No.: 59-50-7
Lot No.: ASL1407
- Purity: 100%
- Supplier: Wako Pure Chemical Industries, Ltd.
- Boiling point : 235°C
- Melting point/Freezing point: 65.7°C
- Vapor pressure: 0.05 mmHg (20°C)
- Solubility: 1 g/260 mL (20°C) in water.
- Physical state: white powder
- Storage condition of test material: stored at room temperature (21.1-25.3°C), light shielding

Method

Species / strain

Species / strain
other:

Details on mammalian cell lines (if applicable)
Chinese hamster lung(CHL/IU) cells

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
Preliminary study
50, 500, 5000 µg/mL (100% growth inhibition was observed at 500 µg/mL and higher)
Main study
[short-term treatment (6 h)] (+/-S9 mix): 50, 100, 200, 300, 400, 500 µg/mL
[continuous treatment (24 h)]: 50, 100, 150, 200, 250, 300 µg/mL

Vehicle
DMSO

Controls

Negative controls
no

Solvent controls
yes

True negative controls
no

Positive controls
yes

Positive control substance
benzo(a)pyrene
+S9 mix
mitomycin C
-S9 mix

Details on test system and conditions
METHOD OF APPLICATION: Exposure duration: [short-term treatment]:6 hrs + 18 hr, [continuous treatment]: 24h
STAIN: Giemsa stain (3 v/v%) for 10 min.
NUMBER OF REPLICATIONS: 2
NUMBER OF CELLS EVALUATED: 1000 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.
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
Not used

Results and discussion

Test results

Key result
false

Species / strain
other: Chinese hamster lung(CHL/IU) cells

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity
yes

Vehicle controls valid
yes

Negative controls valid
not examined

Positive controls valid
yes

Additional information on results
Figures and Tables (in Japanese) are available in the following full report of the study. http://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF59-50-7f.pdf

Tables (in English) are attachted to this document. Please download the export file to see the Tables.

Applicant's summary and conclusion

Conclusions
Negative with and without metabolic activation

Executive summary

The in vitro chromosomal aberration test using CHL/IU cells (OECD TG 473) was negative with and without metabolic activation.

Toxicity to reproduction

ENDPOINT_STUDY_RECORD: Toxicity to reproduction.001

UUID: 1bfb91e5-1962-41d1-b12b-a748fd549888
Dossier UUID:
Author: Dra
Date: 2018-03-30T09:01:58.665+09:00
Remarks:

Administrative data

Endpoint
screening for reproductive / developmental toxicity

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
Reliability 1

Data source

Reference

A reproduction/developmental toxicity screening test in rats treated orally with 4-chloro-m-cresol / Ministry of Health, Labor and Welfare, Japan / study report

Data access
data published

Materials and methods

Test guideline

Qualifier
according to

Guideline
OECD Guideline 421 (Reproduction / Developmental Toxicity Screening Test)

Deviations
no

GLP compliance
yes

Test material

Specific details on test material used for the study
- Name of test material (as cited in study report): 4-Chloro-m-cresol
- Analytical purity: 99.9%
- Storage condition of test material: at a cold (temperature 1-8 °C) and dark place, with airtight sto pper.
- Stability under test conditions: The stability of test material was identified by analysis of the remainder.

Test animals

Species
rat

Strain
other: Crl:CD(SD)

Sex
male/female

Details on test animals and environmental conditions
TEST ANIMALS
- Source: Charle s River Japan, Inc., Atsugi Breeding Center.
- Age at study initiation: 10 weeks
- Weight at study initiation: Male: 398.6 g (366 -432 g), Female: 257.2 g (235-283 g)
- Housing: Animals were housed individually, except for during the acclimation (two animals by sex), mating (one male and one female) and lactation periods (one litter), in metallic bracket-type cages with wire mesh floors (260 mm x 380 mm x 180 mm). From gestation day 17 to lactation day 4, indivi dual dams and litters were reared on bedding.
- Diet: Solid feed (CRF-1: Oriental Yeast Co., ltd.) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation period: 14 days

ENVIRONMENTAL CONDITIONS
- Temperature (°C): 22±3 (actual temperature: 21-25°C)
- Humidity (%): 50±20% (actual humidity: 36-62%)
- Air changes (per hr): 10-15
- Photoperiod (hrs dark / hrs light): 12 hr dark/12 hr light (light: 8:00~20:00)

Administration / exposure

Route of administration
oral: gavage

Vehicle
corn oil

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

- After 14 days of unsuccessful pairing replacement of first male by another male with proven fertility.

Analytical verification of doses or concentrations
yes

Details on analytical verification of doses or concentrations
- Amount of vehicle (if gavage): 5 mL/kg
- Dosing volume: 5 mL/kg

Duration of treatment / exposure
(P) Males: 42 days including 14 days pre-mating and mating periods, and thereafter 14 days (P) Females: up to 56 days including 14 days pre-mating, mating and gestation periods, and the days until day 3 of lactation

Frequency of treatment
Once/day, 7days/week

Doses / concentrations

Dose / conc.	
0	mg/kg bw/day (actual dose received)
Dose / conc.	
35	mg/kg bw/day (actual dose received)
Dose / conc.	
150	mg/kg bw/day (actual dose received)
Dose / conc.	
600	mg/kg bw/day (actual dose received)

No. of animals per sex per dose
12 animals/sex/dose

Control animals
yes, concurrent vehicle

Details on study design
- Dose selection rationale: Based on the results of a 14-day preliminary study, the highest dose of 600 mg/kg bw/day was selected as an expected obvious toxic dose, and the lowest dose of 35 mg/kg bw /day was selected as an expected no toxic dose. The middle dose levels of 150 mg/kg bw/day were selected.
- Rationale for animal assignment (if not random): Body weight-balanced randomization

[14-day preliminary study]
A 14-day repeated dose oral toxicity test (Crl:CD(SD) rats, doses: 0 (olive oil), 35, 150, and 600 mg/kg bw/day). At 600 mg/kg bw/day, staggering gait, soiled perineal region, yellowish white mass in the cauda epididymis were observed.

Examinations

Parental animals: Observations and examinations
CAGE SIDE OBSERVATIONS: Yes
- Time schedule: Males and females: 2 times/day

BODY WEIGHT: Yes
- Time schedule for examinations:
Males: Days 1, 2, 5, 7, 10, 14, 21, 28, 35, 42, and the day of necropsy
Females: Days 1, 2, 5, 7, 10, and 14; gestation days 0, 1, 3, 5, 7, 10, 14, 17, and 20; lactation days 0, 1 and 4; and the day of necropsy. For unmating females, 21 and 28 in the mating period

FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):
- Food consumption: Yes
Males: Days 1, 2, 5, 7, 10, 14, 21, 28, 35, and 42, in dosing period
Females: Days 1, 2, 5, 7, 10, and 14; gestation days 0, 1, 3, 5, 7, 10, 14, 17, and 20; lactation days 0, 1 and 4
OTHER: Females: Numbers of corpus luteum and implantation site on the day of necropsy

Estrous cyclicity (parental animals)
Vaginal smears were collected from all females and microscopically examined every day from the day after the start of administration until the day copulation was confirmed.
During the pre-mating administration period, vaginal smear pictures were classified as proestrus, estrus, metestrus or diestrus and examined for the frequency of estrus and interval between estruses (estrous cycle). During the mating period, vaginal smears were examined for the presence of sperm.

Sperm parameters (parental animals)
Parameters examined in P male parental generations: testis weight, epididymis weight

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, weigh t.

GROSS EXAMINATION OF DEAD PUPS: Yes, for external and internal abnormalities.

Postmortem examinations (parental animals)
SACRIFICE
- Male animals: All surviving animals were euthanized by exsanguination under ether anesthesia on t he day after the last administration.
- Maternal animals: All surviving animals were euthanized by exsanguination under ether anesthesia on day 4 of lactation.

GROSS NECROPSY: Yes (gross necropsy consisted of external and internal examinations including the cervical, thoracic, and abdominal viscera.)

HISTOPATHOLOGY: Yes (Male: testis, epididymis, and gross abnormal site (ileum); Female: ovary, and gross abnormal site (pituitary gland, thymus, spleen, kidney, ileum))

ORGAN WEIGHTS: Yes (brain, thymus, heart, liver, kidney, spleen, adrenal, testis, epididymis, ovary)

Postmortem examinations (offspring)
SACRIFICE
- The F1 pups were euthanized on day 4 of lactation by using carbon dioxide.

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

Statistics
Body weights, body weight gain, food consumption, organ weights and relative organ weights, stages of spermatogenesis, length of the estrous cycle, number of corpora lutea, number of implantation sites, implantation index, delivery index, number of pups delivered, number of live pups, live birth index, sex ratio, number of live pups and viability index at lactation day4 were analyzed for statistical significance in the following way: homogeneity of variance was evaluated first by Bartlett's test. When group variances were homogeneous, the one-way analysis of variance was used to determine if any statistical differences existed among the groups. If the analysis of variance gave a significant result, Dunnett's test was performed to detect any significant differences between the treated groups and their corresponding controls. When Bartlett's test indicated that the variances were not homogeneous, the Kruskal-Wallis test was used for detecting any statistical differences and if they were significant, the Mann-Whitney U test was performed to detect any significant differences between the treated groups and their corresponding controls. The incidences of females with abnormal estrous cyclicity, and indices of copulation, fertility and gestation, and nursing index were analyzed by the Chi-square test or Fisher's exact probability test.

Reproductive indices
Each parameter was determined by the following equations:
Abnormal estrous cycle = (No. of female with abnormal estrous cycle/No. of females examined) × 100
Copulation index (%) = (No. of animals with successful copulation/No. of animals mated) × 100
Fertility index (%) = (No. of pregnant females/No. of pairs with successful copulation) × 100
Gestation index (%) = (No. of females with live pups/number of pregnant females) × 100
Nursing index (%) = (No. of females nursing live pups on lactation day 4/No. of females with live pups delivery) × 100
Implantation index (%) = (No. of implantation sites/No. of corpora lutea) × 100
Delivery index (%) = (No. of pups born/No. of implantation sites) × 100
Sex ratio = No. of live male pups/No. of live pups
Live birth index (%) = (No. of live pups on lactation day 0/No. of pups born) × 100

Offspring viability indices
Viability index on lactation day 4 = (No. of live pups on lactation day 4/No. of live pups on lactation day 0) × 100

Results and discussion

Results: P0 (first parental animals)

General toxicity (P0)

Clinical signs
effects observed, treatment-related

Description (incidence and severity)
see 7.5.1 Repeated dose toxicity: oral.002

Mortality
no mortality observed

Body weight and weight changes
effects observed, treatment-related

Description (incidence and severity)
see 7.5.1 Repeated dose toxicity: oral.002

Food consumption and compound intake (if feeding study)
effects observed, treatment-related

Description (incidence and severity)
see 7.5.1 Repeated dose toxicity: oral.002

Food efficiency
not examined

Water consumption and compound intake (if drinking water study)
not examined

Ophthalmological findings
not examined

Haematological findings
not examined

Clinical biochemistry findings
not examined

Urinalysis findings
not examined

Behaviour (functional findings)
not examined

Immunological findings
not examined

Organ weight findings including organ / body weight ratios
effects observed, treatment-related

Description (incidence and severity)
see 7.5.1 Repeated dose toxicity: oral.002
no effects on reproductive organs

Gross pathological findings
no effects observed

Description (incidence and severity)
no effects on reproductive organs

Neuropathological findings
not examined

Histopathological findings: non-neoplastic
no effects observed

Description (incidence and severity)
no effects on reproductive organs

Histopathological findings: neoplastic
not examined

Reproductive function / performance (P0)

Reproductive function: estrous cycle
no effects observed

Reproductive function: sperm measures
effects observed, non-treatment-related

Description (incidence and severity)
Increase number of cells on preleptotene spermatocytes at Stage VII-VIII at 600 mg/kg bw/day.

Reproductive performance
no effects observed

Effect levels (P0)

Key result
true

Dose descriptor
NOAEL

Effect level

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

Based on
test mat.

Sex
male/female

Results: F1 generation

General toxicity (F1)

Clinical signs
no effects observed

Mortality / viability
mortality observed, non-treatment-related

Description (incidence and severity)
control: 2 males and 4 females died.
35 mg/kg bw/day: 2 males died.
150 mg/kg bw/day: 3 males and 2 females died.
600 mg/kg bw/day: 2 males and 1 females died.

Body weight and weight changes
no effects observed

Sexual maturation
not examined

Organ weight findings including organ / body weight ratios
not examined

Gross pathological findings
no effects observed

Histopathological findings
not examined

Effect levels (F1)

Key result
true

Dose descriptor
NOAEL

Generation
F1

Effect level

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

Based on
test mat.

Sex
male/female

Any other information on results incl. tables

Figures and Tables (in English) are available in the following full report of the study.

http://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF59-50-7c.pdf

Applicant's summary and conclusion

Executive summary

A reproduction/developmental toxicity screening test was performed according to OECD TG 421. Male and female rats (12 animals/sex/dose) were administered 4 -chloro-m-cresol at 0, 35, 150, and 600 mg/kg bw/day. Males were dosed for 42 days, including a 14 day pre-mating and mating periods. Females were dosed for 56 days, including a 14 day pre-mating, mating, and gestation periods, and the time until lactation day 3. No effects of this substance on reproductive and developmental parameters were observed at 600 mg/kg bw/day. NOAEL for the rat reproductive/developmental toxicity of 4 -chloro-m-cresol was determined to be 600 mg/kg bw/day, the highest dose tested.

References

REFERENCE_SUBSTANCE: 4-chloro-m-cresol

UUID: fa2f9d53-ba31-416b-964a-93e8166287ef
Dossier UUID:
Author: Dra
Date: 2018-02-27T14:37:55.390+09:00
Remarks:

General information

Reference substance name
4-chloro-m-cresol

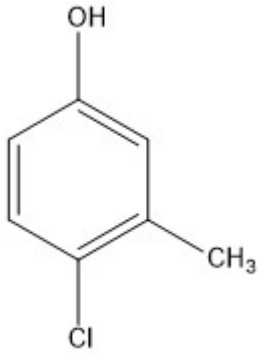
Reference substance information

CAS information

CAS number
59-50-7

Molecular and structural information

Structural formula



LITERATURE: A reproduction/developmental toxicity screening test in rats treated orally with 4-chloro-m-cresol

UUID: 01a49291-8a84-4bfd-80d1-76819202e03a
Dossier UUID:
Author: Dra
Date: 2018-03-14T15:23:19.000+09:00
Remarks:

General information

Reference Type
study report

Title
A reproduction/developmental toxicity screening test in rats treated orally with 4-chloro-m-cresol

Author
Ministry of Health, Labor and Welfare, Japan

Bibliographic source
available in the web of Japan Existing Chemical Data Bae (JCEDB) at

Testing facility
Safety Research Institute for Chemical Compounds Co., Ltd.

Report no.
SR08135

LITERATURE: In Vitro Chromosomal Aberration Test of 4-chloro-m-cresol on Cultured Chinese Hamster Cells

UUID: 073bdd8b-cbe0-45d4-92e8-d80334293bb1
Dossier UUID:
Author: Dra
Date: 2018-02-27T16:54:46.649+09:00
Remarks:

General information

Reference Type
study report

Title
In Vitro Chromosomal Aberration Test of 4-chloro-m-cresol on Cultured Chinese Hamster Cells

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

Year
2007

Bibliographic source
Japan Existing Chemical Data Base (JECDB) http://dra4.nihs.go.jp/mhlw_data/jsp/SearchPageENG.jsp

Testing facility
Mitsubishi Safety Institute Ltd.

Report no.
B060313

LEGAL_ENTITY: National Institute of Health Sciences

UUID: IUC4-b036ff75-0f3c-323b-b200-ed5f46cf5101

Dossier UUID:

Author: SuperUser

Date: 2019-09-03T10:05:28.255+09:00

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 official MHLW opinions or any other regulatory policies.

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 official MHLW opinions or any other regulatory policies.

Identifiers

Other IT system identifiers

IT system
LEO

ID
10767

IT system
IUCLID4

ID
16558402024DIV750

Contact information

Contact address

Address 1
Tonomachi 3-25-26

Address 2
Kawasaki-ku

Postal code
210-9501

Town
Kawasaki

Region / State
Kanagawa

Country
Japan

Contact persons

Person
Hirose, Akihiko; National Institute of Health Sciences, Japan

Last name
Hirose

First name
Akihiko

Organisation
National Institute of Health Sciences, Japan

Department
Division of Risk Assessment

Title
Dr

Country
Japan

LITERATURE: Reverse Mutation Test of 4-chloro-m-cresol on Bacteria

UUID: 6c7ed821-3dcf-4cf8-84b3-97085910a4cb
Dossier UUID:
Author: Dra
Date: 2018-02-27T16:44:27.228+09:00
Remarks:

General information

Reference Type
study report

Title
Reverse Mutation Test of 4-chloro-m-cresol on Bacteria

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

Year
2007

Bibliographic source
Japan Existing Chemical Data Base (JECDB) http://dra4.nihs.go.jp/mhlw_data/jsp/SearchPageENG.jsp

Testing facility
Mitsubishi Safety Institute Ltd.

Report no.
B060312

LITERATURE: Twenty-eight-day Repeat D ose Oral Toxicity Test of 4-chloro-m-cresol in Rats

UUID: 4e3fff29-f57b-43c3-a2f7-968da6f2a134
Dossier UUID:
Author: Dra
Date: 2018-03-17T12:37:49.000+09:00
Remarks:

General information

Reference Type
study report

Title
Twenty-eight-day Repeat Dose Oral Toxicity Test of 4-chloro-m-cresol in Rats

Author
Ministry of Health, Labor and Welfare, Japan

Bibliographic source
available in the web of Japan Existing Chemical Data Bae (JCEDB) at

Testing facility
Research Institute for Animal Science in Biochemistry and Toxicology

Study no.
06-087