Name: COMPLETE / SUBSTANCE : Polyoxyethylenesorbitan fatty acid(C12-18)ester / 9005-70-3 Tue, 5 Sep 2023, 13:41:03+0900 /

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

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Remarks:

Dossier header

Dossier submission type

Name
Complete table of contents

Version
core 8.0

Name (given by user)

Dossier subject

Dossier subject
Polyoxyethylenesorbitan fatty acid(C12-18)ester / 9005-70-3

Public name

Submitting legal entity
National Institute of Health Sciences / Kawasaki / Japan

Dossier creation date/time
Tue, 5 Sep 2023, 13:41:03+0900

Used in category

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.

Address

Address 1
Tonomachi 3-25-26

Address 2
Kawasaki-ku

Postal code
210-9501

Town
Kawasaki

Region / State
Kanagawa

Country
Japan
JP

Identifiers

Other IT system identifiers

IT system
LEO

ID
10767

IT system
IUCLID4

ID
16558402024DIV750

Polyoxyethylenesorbitan fatty acid(C12-18)ester

OECD

Health Effects

Repeated dose toxicity: oral

ENDPOINT_STUDY_RECORD: RepeatedDoseToxicityOral.001

UUID: 31d811f0-c059-4cc9-9031-cad977423626
Dossier UUID:
Author:
Date: 2022-03-25T15:24:50.000+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
guideline study OECD Test Guideline study under GLP condition
Reliability 1

Cross-reference

Reason / purpose for cross-reference
reference to same study

Related information
OECD / Toxicity to reproduction / ToxicityReproduction.001 / Polyoxyethylenesorbitan fatty acid(C12-18)ester / 9005-70-3

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 https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF9005-70-3d.pdf

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
no

GLP compliance
yes

Limit test
no

Test material

Test material information
Polyoxyethylenesorbitan fatty acid(C12-18)ester

Specific details on test material used for the study
- Name of test material (as cited in study report): Polyoxyethylene sorbitan trioleate
- CAS No.: 9005-70-3
- Analytical purity: -
- Storage condition of test material: Room temperature, shading, airtightness
- Stability under test conditions: The stability of test material was identified by analysis of the remainder.

Test animals

Species
rat
common rodent species

Strain
other: Crl: CD (SD)

Sex
male/female

Details on test animals or test system and environmental conditions
TEST ANIMALS
- Source: Charles River Japan, Inc., Hino Breeding Center.
- Age at study initiation: 10 weeks old
- Weight at study initiation:

Males (main study groups): 357-412 g, females (main study groups): 226-265 g, females (mating stu dy groups): 211-255 g
- Housing: Animals were individually housed in stainless steel suspension cage (240W × 380D × 200H mm), from gestation day 18 to lactation day 4, Dams were bred individually or with individual litte rmates in plastic cages (310W x 360D x 175H mm) and bedding.
- Diet: Solid feed (CRF-1: Oriental Yeast Co., ltd.) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation period: Males (main study groups): 19 days, females (main study groups): 20 days, females (mating study groups): 19 days

ENVIRONMENTAL CONDITIONS
- Temperature (°C): 20-26°C (actual temperature: 22.3-24.3°C)
- Humidity (%): 40.0-70.0% (actual humidity: 40.6-65.9%)
- Air changes (per hr): 12
- Photoperiod (hrs dark / hrs light): 12 hr dark/12 hr light (light: 6:00-18:00)

Administration / exposure

Route of administration
oral: gavage

Vehicle
water water for injection

Details on oral exposure
- Amount of vehicle (if gavage): 10 mL/kg
- Dosing volume: 10 mL/kg

Analytical verification of doses or concentrations
yes

Details on analytical verification of doses or concentrations
The concentrations of each test solution using administration on day 1 were analyzed with a spectrop hotometer. Results showed that the concentrations of each test solution were 98.7 to 103.7% of the nominal concentration and both values were within the acceptable range (concentration: percentage of nominal concentration, 100±10%)

Duration of treatment / exposure
Males: 28 days including 14 days pre-mating
Females (main study groups): 28 days
Females (mating study groups): 42-54 days including 14 days pre-mating, mating and gestation period s and the days until day 4 of lactation

Frequency of treatment
Once/day, 7 days/week

Doses / concentrations

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

Dose / conc.	
62.5	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
- Main study:
Control- and high-dose groups: 12 males and 10 females per group (half of both sexes assigned as the treatment groups, and the remaining half assigned as the recovery groups)
Low -and middle-dose groups: 12 males and 5 females per group (half of males assigned as the treatment groups, and the remaining half assigned as the recovery groups)

- Mating study:
12 females per dose

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 1000 mg/kg bw/day, which is the upper limit in OECD TG422, and the intermediate dose and low dose were set to 250 mg/kg bw/day and 62.5 mg/kg bw/day, respectively.

[14-day preliminary study]
A 14-day repeated dose oral toxicity test (Crl:CD(SD) rats, doses: 0, 200, 500 or 1000 mg/kg bw/day).
No effects of the test substance were observed in males and females up to the 1000 mg/kg/day dose group.

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

Examinations

Observations and examinations performed and frequency
CAGE SIDE OBSERVATIONS: Yes
- Time schedule:
Males and females (main study groups): 2 times/day (before administration, 61-189 minutes after administration) during the administration period. Once a day during the recovery period.
Females (mating study groups): 2 times/day (before administration, 60-211 minutes after administrat ion) during the administration period.
DETAILED CLINICAL OBSERVATIONS: Yes
- Time schedule:
Males and females (main study groups): on day of grouping, on days 7, 14, 21 and 27 of administra tion period.
Females (mating study groups): on day of grouping, on days 7 and 14 of administration period, on days 1, 8 and 15 of gestation period, on day 4 of lactation period.

BODY WEIGHT: Yes
- Time schedule for examinations:
Males and females (main study groups):
Twice a week (On days 1, 4, 8, 11, 15, 18, 22, 25, 28 and 29 of administration period, on days 1, 4, 8, 11, 14 and 15 of recovery period).
Females (mating study groups): Twice a week (On days 1, 4, 8, 11, 15 and 18 of administration period, on days 0, 7, 14 and 20 of gestation period, on days 0, 4 and 5 of lactation period).

FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):
- Food consumption: Yes
- Time schedule for examinations:
Males and females (main study groups):
Twice a week (Males: On days 2, 5, 9 and 12 of administration period, on days 2, 5, 9 and 12 of rec overy period; Females: On days 2, 5, 9, 12, 16, 19, 23 and 26 of administration period, on days 2, 5, 9 and 12 of recovery period).
Females (mating study groups): Twice a week (On days 2, 5, 9 and 12 of administration period, on d ays 2, 9, 16 and 20 of gestation period, on days 2 of lactation period).

WATER INTAKE: Yes
- Time schedule for examinations:
Males and females (main study groups):
Twice a week (Males: On days 2, 5, 9 and 12 of administration period, on days 2, 5, 9 and 12 of recovery period; Females: On days 2, 5, 9, 12, 16, 19, 23 and 26 of administration period, on days 2, 5, 9 and 12 of recovery period).
Females (mating study groups): Twice a week (On days 2, 5, 9 and 12 of administration period, on days 2, 9, 16 and 20 of gestation period, on days 2 of lactation period).

OPHTHALMOSCOPIC EXAMINATION: No
HAEMATOLOGY: Yes
- Time schedule for collection of blood:
Males and females (main study groups): At the end of administration period, or at the end of recovery period in both sexes
- Anaesthetic used for blood collection: Pentobarbital sodium
- Animals fasted: Yes
- How many animals:
At the end of administration period: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0, 62.5, 250, 1000 mg/kg bw/day)
At the end of recovery period: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0 and 1000 mg/kg bw/day)
- Parameters examined: red blood cell count, hemoglobin, hematocrit, mean corpuscular volu me, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, reticulocyte p ercentage, platelet count, white blood cell count, differential white blood cell count, prothrombin time, activated partial thromboplastin time, fibrinogen.

CLINICAL CHEMISTRY: Yes
- Time schedule for collection of blood:
Males and females (main study groups): 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: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0, 62.5, 250, 1000 mg/kg bw/day)
At the end of recovery period: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0 and 1000 mg/kg bw/day)
- Parameters checked: ALP, total cholesterol, triglyceride, total bilirubin, glucose, urea nitrogen, creati nine, sodium, potassium, chloride, calcium, inorganic phosphorus, total protein, albumin, A/G ratio, AST, ALT, γ-GT

URINALYSIS: Yes
- Time schedule for collection of urine:
Males and females (main study groups): Before the end of the administration period (day 23 of a dministration period) and before the end of recovery (days 12 of recovery period).
- Metabolism cages used for collection of urine: Yes
A urine collector to collect fresh urine samples under fasting but ad libitum drinking conditions, follo wed by collection of 24-hour urine samples under ad libitum feeding and drinking conditions.
- How many animals:

At the end of administration period: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0, 62.5, 250, 1000 mg/kg bw/day)
At the end of recovery period: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0 and 1000 mg/kg bw/day)
- Parameters checked:
Fresh urine: Color, pH, protein, glucose, ketones, bilirubin, occult blood, urobilinogen, sediment
24-urine: Specific gravity, urine volume (24-hour volume)

BLOOD HORMONE: Yes
- Time schedule for collection of serum:
Males and females (main study groups): At the end of administration period in both sexes
- Animals fasted: Yes
- How many animals:
6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0, 62.5, 250, 1000 mg/kg bw/day)
- Parameters checked: Triiodothyronine (T3), Thyroxin (T4), and thyroid stimulating hormone (TSH)

NEUROBEHAVIOURAL EXAMINATION: Yes
- Time schedule for examinations:
Males and females (main study groups): Final week of administration (Manipulative test and measurement of grip strength: Day 27 of administration, measurement of motor activity: Day 26 of administration)
- Dose groups that were examined: Autopsy animals after the end of the administration period
- Battery of functions tested:
1) Manipulative Test. Pupillary reflex, approaching behavior, response to touch, auditory reflex, pain reflex
2) Measurement of Grip Strength. Following manipulative test, grip strength of forelimb and hind limb were measured by CPU gauge (San Diego Instruments Inc.).
3) Measurement of Spontaneous Motor Activity. Spontaneous motor activity (Ambulatory and vertical counts) was measured by Activity Monitor (MED Associates Inc.).
The measurements were collected at 10-minute intervals from 1 hour to 2 hours after administration.

Sacrifice and pathology
GROSS PATHOLOGY: Yes
ORGAN WEIGHT: Yes [main study groups: brain, pituitary, salivary glands, thyroids, adrenal gland, thymus, spleen, heart, liver, kidney, testes, epididymides, ventral prostate, seminal vesicles, ovaries, uterus; females in mating group: ovary, uterus]
HISTOPATHOLOGY: Yes, [main study groups: heart, lung, trachea, liver, pancreas, sublingual gland, submandibular gland, esophagus, stomach, duodenum, jejunum, ileum (including Peyer’s patch), cecum, colon, rectum, thymus, spleen, mandibular lymph nodes, mesenteric lymph nodes, kidney, urinary bladder, testis, epididymis, ventral prostate, seminal vesicles (including coagulating gland), ovaries, uterus, vagina, pituitary, adrenal glands, thyroid (including parathyroid), cerebrum, cerebellum, pons, spinal cord, sciatic nerve, eye ball, Harderian gland, sternum and femur (including bone marrows), muscle (rectus femoris), mammary gland; females in mating group: ovaries, uterus, vagina]

Statistics
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 Steel method. For comparison of quantitative data between two groups in the 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.
Regarding clinical observation (except for frequency of urination, defecation, rearing and grooming) and sensory reactivity, Steel test was applied.

Results and discussion

Results of examinations

Clinical signs
no effects observed

Mortality
no mortality observed

Body weight and weight changes
no effects observed

Food consumption and compound intake (if feeding study)
no effects observed

Food efficiency
not examined

Water consumption and compound intake (if drinking water study)
no effects observed

Ophthalmological findings
not examined

Haematological findings
effects observed, treatment-related

Clinical biochemistry findings
no effects observed

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

Gross pathological findings
no effects observed

Neuropathological findings
not examined

Histopathological findings: non-neoplastic
no effects observed

Histopathological findings: neoplastic
not examined

Details on results
CLINICAL SIGNS AND MORTALITY:
Mortality: There was no death.
Clinical signs: There were no changes related to the test substance in any groups at the dosing and recovery periods.

DETAILED CLINICAL OBSERVATIONS:
There were no changes related to the test substance in any groups at the dosing and recovery perio ds.

BODY WEIGHT:
There were no changes related to the test substance in any groups at the dosing and recovery periods.
FOOD CONSUMPTION:
There were no changes related to the test substance in any groups at the dosing and recovery periods.

WATER CONSUMPTION:
There were no changes related to the test substance in any groups at the dosing and recovery period s.

URINALYSIS:
There were no changes related to the test substance in any groups at the dosing and recovery p eriods.

HAEMATOLOGY:
[At the end of dosing period]: Decreases in hematocrit and hemoglobin were observed in females at 1000 mg/kg bw/day.
[At the end of recovery period]: There were no changes related to the test substance in any groups.
CLINICAL CHEMISTRY (Including blood hormones (T3, T4, TSH)):
There were no changes related to the test substance in any groups at the end of dosing and recovery periods.

NEUROBEHAVOURAL EXAMINATION:
1) MANIPULATIVE TEST:
There were no changes related to the test substance in any groups at the dosing and recovery pe riods.
2) GRIP STRENGTH TEST:
There were no changes related to the test substance in any groups at the dosing and recovery period s.
3) LOCOMOTOR ACTIVITY MEASUREMENT:
There were no changes related to the test substance in any groups at the dosing and recovery periods.

ORGAN WEIGHTS:
[At the end of dosing period]: Increases in absolute and relative liver weights, an increase in absolute adrenal weight and an increase tendency in relative adrenal weight were observed in females at 1000 mg/kg bw/day.
[At the end of recovery period]: There were no changes related to the test substance in any groups.

GROSS PATHOLOGY:
There were no changes related to the test substance in any groups at the end of dosing and recovery periods.

HISTOPATHOLOGY: NON-NEOPLASTIC:
There were no changes related to the test substance in any groups at the end of dosing and recovery periods.

Effect levels

Key result
false

Dose descriptor
NOAEL

Effect level

1000 mg/kg bw/day (actual dose received)

Based on
test mat.

Sex
male

Basis for effect level
other:
No toxic effects were observed in males up to the highest dose of 1000 mg/kg bw/day.

Key result
false

Dose descriptor
NOAEL

Effect level

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

Based on
test mat.

Sex
female

Basis for effect level
haematology
Decreases in hematocrit and hemoglobin were observed in females at 1000 mg/kg bw/day.
organ weights and organ / body weight ratios
Increases in absolute and relative liver weights, an increase in absolute adrenal weight and an incr ease tendency in relative adrenal weight were observed in females at 1000 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.

https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF9005-70-3d.pdf

Applicant's summary and conclusion

Conclusions
The NOAEL for repeated dose toxicity in this study was determined to be 1000 and 250 mg/kg bw/day for males and females, respectively.

Executive summary

In the combined repeated dose and reproductive/developmental screening test (OECD TG422), SD rats were treated orally with polyoxyethylenesorbitan fatty acid(C12-18)ester at the doses of 0, 62.5, 250 and

1000 mg/kg bw/day. Males (12 animals/dose: 6 animals were treated as a recovery group) were dosed for 28 days including a 14 day pre-mating period. Females (12 animals/dose) were dosed for 42-46 days including 14 day premating, mating, and gestation periods and days until day 4 of lactation. In addition, as the main study group of females, 5 or 10 females/group was dosed for 28 days without mating (5 females were treated at 0 and 1000 mg/kg bw/day as recovery groups).

The following findings were observed in the examination at the end of the administration period. In the haematology, decreases in hematocrit and hemoglobin were observed in females at 1000 mg/kg bw/day. In the organ weight, increases in absolute and relative liver weights, an increase in absolute adrenal weight, and an increase tendency in relative adrenal weight were observed in females at 1000 mg/kg bw/day. On the other hand, no toxic effects were observed in males up to the highest dose of 1000 mg/kg bw/day. Based on the above results, the NOAEL for the repeated dose toxicity of polyoxyethylenesorbitan fatty acid(C12-18)ester was determined to be 1000 and 250 mg/kg bw/day for males and female rats, respectively.

Genetic toxicity in vitro

ENDPOINT_STUDY_RECORD: Genetic toxicity in vitro.001

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Dossier UUID:	
Author:	
Date:	2022-03-25T15:25:17.000+09:00
Remarks:	

Administrative data

Endpoint
in vitro gene mutation study in bacteria

Type of information
experimental study

Adequacy of study
key study

Robust study summary
false

Used for classification
false

Used for SDS
false

Reliability
1 (reliable without restriction)

Rationale for reliability incl. deficiencies
other: OECD Test Guideline study under GLP condition

Data source

Reference

Reverse Mutation Test of Polyoxyethylene sorbitan trioleate 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
not specified

Qualifier
according to guideline

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

Deviations
not specified

GLP compliance
yes

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

Test material

Test material information
Polyoxyethylenesorbitan fatty acid(C12-18)ester

Specific details on test material used for the study
- Name of test material (as cited in study report): Polyoxyethylene sorbitan trioleate
- CAS No.: 9005-70-3
- Analytical purity: -
- Storage condition of test material: Room temperature, shading, airtightness
- Stability under test conditions: The stability of test material was identified by analysis of the remainder.

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
bacteria

Metabolic activation
with and without

Metabolic activation system
S9 mix; SD male rat liver, induced by phenobarbital and 5,6-benzoflavone

Justification for deviation from the high dose level
-S9 mix:

312.5, 625, 1250,2500, 5000 µg/plate (TA100, TA1535, WP2uvrA, TA98, TA1537 strains)
+S9 mix:
312.5, 625, 1250,2500, 5000 µg/plate (TA100, TA1535, WP2uvrA, TA98, TA1537 strains)

Maximum concentration was established based on the result of the preliminary test at concentration up to 5000 ug/plate. In this test, this chemical did not induce gene mutations in S. typhimurium and E. coli strains, and cytotoxicity was not observed in all strains at up to 5000 µg/plate with and without S9 mix.

Vehicle / solvent
- Vehicle(s)/solvent(s) used: Water for injection

Controls

Untreated negative controls
no

Negative solvent / vehicle controls
yes

True negative controls
no

Positive controls
yes

Positive control substance
other: -S9 mix: 2-(2-furyl)-3-(5-nitro-2-furyl) acrylamide (AF-2), sodium azide (NaN3), 9-aminoacridine hydrochloride (9AA);
+S9 mix: 2-aminoanthracene (2AA)

Details on test system and experimental conditions
METHOD OF APPLICATION: Preincubation
DURATION- Preincubation period: 20 min at 37°C
- Exposure duration:48 hrs
NUMBER OF PLATES: 3
NUMBER OF REPLICATIONS: 1
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 nor precipitates, but tested up to recommended limit concentrations

Vehicle controls validity
valid

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 nor precipitates, but tested up to recommended limit concentrations

Vehicle controls validity
valid

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 nor precipitates, but tested up to recommended limit concentrations

Vehicle controls validity
valid

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 nor precipitates, but tested up to recommended limit concentrations

Vehicle controls validity
valid

Positive controls validity
valid

Key result
true

Species / strain
E. coli WP2 uvr A
bacteria

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity / choice of top concentrations
no cytotoxicity nor precipitates, but tested up to recommended limit concentrations

Vehicle controls validity
valid

Positive controls validity
valid

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/PDF9005-70-3e.pdf

Applicant's summary and conclusion

Conclusions
Interpretation of results (migrated information): negative

In a bacterial reverse mutation assay using Salmonella typhimurium TA100, TA1535, TA98, and TA 1537, and Escherichia coli WP2uvrA (OECD TG 471), polyoxyethylenesorbitan fatty acid(C12-18)ester was negative with or without metabolic activation.

ENDPOINT_STUDY_RECORD: Genetic toxicity in vitro.002

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Dossier UUID:
Author:
Date: 2022-03-25T15:25:46.000+09:00
Remarks:

Administrative data

Endpoint
in vitro 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
other: OECD Test Guideline study under GLP condition

Data source

Reference

In Vitro Chromosomal Aberration Test of Polyoxyethylene sorbitan trioleate on Cultured Chinese Hamst / 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 Chromosome Aberration Test)
in vitro cytogenicity / chromosome aberration study in mammalian cells

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
other: in vitro mammalian chromosome aberration test

Test material

Test material information
Polyoxyethylenesorbitan fatty acid(C12-18)ester

Specific details on test material used for the study
- Name of test material (as cited in study report): Polyoxyethylene sorbitan trioleate
- CAS No.: 9005-70-3
- Analytical purity: -
- Storage condition of test material: Room temperature, shading, airtightness
- Stability under test conditions: The stability of test material was identified by analysis of the remainder.

Method

Species / strain

Species / strain / cell type
other: 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

Justification for deviation from the high dose level
Cell growth inhibition study
-S9 mix (short-term treatment): 33.6, 67.2, 134.4, 268.8, 537.5, 1075, 2150, 4300 ug/mL
+S9 mix (short-term treatment): 33.6, 67.2, 134.4, 268.8, 537.5, 1075, 2150, 4300 ug/mL
-S9 mix (continuous treatment, 24hr): 33.6, 67.2, 134.4, 268.8, 537.5, 1075, 2150, 4300 ug/mL

Main study
-S9 (short-term treatment): 62.5, 125, 250, 500 ug/mL
+S9 (short-term treatment): 62.5, 125, 250, 500 ug/mL
-S9 (continuous treatment, 24hr): 31.3, 62.5, 125, 250 ug/mL

Vehicle / solvent
- Vehicle(s)/solvent(s) used: Water for injection

Controls

Untreated negative controls
no

Negative solvent / vehicle controls
yes

True negative controls
no

Positive controls
yes

Positive control substance
other: [-S9]: mitomycin C; [+S9]: N-dimethylnitrosamine

Details on test system and experimental conditions
METHOD OF APPLICATION:
Exposure duration:
- [short-term treatment]: 6 hrs + 18 hrs
- [continuous treatment]: 24 hrs
SPINDLE INHIBITOR: Colcemid
STAIN: Giemsa stain (2 v/v%) for 15 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(±): more than 5% and less than 10%, Positive(+): 10% and above

Statistics
no

Results and discussion

Test results

Key result
true

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

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity / choice of top concentrations
cytotoxicity

Vehicle controls validity
valid

Positive controls validity
valid

Additional information on results
RANGE-FINDING/SCREENING STUDIES (if applicable):
50% cell growth inhibition (IC50): 340 ug/mL (short-term treatment, +S9 mix), 370 ug/mL (short-term t reatment, -S9 mix), 190 ug/mL (continuous treatment)

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/PDF9005-70-3f.pdf

Applicant's summary and conclusion

Conclusions
Interpretation of results (migrated information): negative with or without metabolic activation

In an in vitro chromosomal aberration test using CHL/IU cells (OECD TG 473), polyoxyethylenes orbitan fatty acid(C12-18)ester was negative with or without metabolic activation.

Toxicity to reproduction

ENDPOINT_STUDY_RECORD: ToxicityReproduction.001

UUID:	8cf29cfa-a458-46fc-84f1-4e868dd8a6ef
Dossier UUID:	
Author:	
Date:	2022-03-25T15:36:47.000+09:00
Remarks:	

Administrative data

Endpoint
reproductive toxicity, other A combined repeated dose/reproductive developmental toxicity study

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 OECD Test Guideline study under GLP condition
Reliability 1

Cross-reference

Reason / purpose for cross-reference
reference to same study

Related information
OECD / Repeated dose toxicity: oral / RepeatedDoseToxicityOral.001 / Polyoxyethylenesorbitan fatty acid(C12-18)ester / 9005-70-3

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
no

GLP compliance
yes

Limit test
no

Test material

Test material information
Polyoxyethylenesorbitan fatty acid(C12-18)ester

Specific details on test material used for the study
- Name of test material (as cited in study report): Polyoxyethylene sorbitan trioleate
- CAS No.: 9005-70-3
- Analytical purity: -
- Storage condition of test material: Room temperature, shading, airtightness
- 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 or test system and environmental conditions
TEST ANIMALS
- Source: Charles River Japan, Inc., Hino Breeding Center.
- Age at study initiation: 10 weeks old
- Weight at study initiation: Males in main group male: 357-412 g, females in main group: 226-265 g, females in mating group: 211-255 g
- Housing: Animals were individually housed in stainless steel suspension cage (240W × 380D × 200H mm), from gestation day 18 to lactation day 4, Dams were bred individually or with individual littermates in plastic cages (310W x 360D x 175H mm) and bedding.
- Diet: Solid feed (CRF-1: Oriental Yeast Co., ltd.) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation period: Males in main group: 19 days, females in main group: 20 days, females in mating group: 19 days

ENVIRONMENTAL CONDITIONS
- Temperature (°C): 20-26°C (actual temperature: 22.3-24.3°C)
- Humidity (%): 40.0-70.0% (actual humidity: 40.6-65.9%)
- Air changes (per hr): 12

- Photoperiod (hrs dark / hrs light): 12 hr dark/12 hr light (light: 6:00-18:00)

Administration / exposure

Route of administration
oral: gavage

Vehicle
water water for injection

Details on exposure
- Amount of vehicle (if gavage): 10 mL/kg
- Dosing volume: 10 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
The concentrations of each test solution using administration on day 1 were analyzed with a spectrop hotometer. Results showed that the concentrations of each test solution were 98.7 to 103.7% of the nominal concentration and both values were within the acceptable range (concentration: percentage of nominal concentration, 100±10%)

Duration of treatment / exposure
Males: 28 days including 14 days pre-mating
Females (main study groups): 28 days
Females (mating study groups): 42-54 days including 14 days pre-mating, mating and gestation period s and the days until day 4 of lactation

Frequency of treatment
Once/day, 7 days/week

Doses / concentrations

Dose / conc.	
0	mg/kg bw/day (actual dose received)
Dose / conc.	
62.5	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
- Main study:
Control- and high-dose groups: 12 males and 10 females per group (half of both sexes assigned as the treatment groups, and the remaining half assigned as the recovery groups)
Low -and middle-dose groups: 12 males and 5 females per group (half of males assigned as the treatment groups, and the remaining half assigned as the recovery groups)

- Mating study:
12 females per dose

Control animals
yes, concurrent no treatment

Details on study design
- Dose selection rationale: Based on the results of a 14-day preliminary study, the high dose was set to 1000 mg/kg bw/day, which is the upper limit in OECD TG422, and the intermediate dose and low dose were set to 250 mg/kg bw/day and 62.5 mg/kg bw/day, respectively.

[14-day preliminary study]
A 14-day repeated dose oral toxicity test (Crl:CD(SD) rats, doses: 0, 200, 500 or 1000 mg/kg bw/day). No effects of the test substance were observed in males and females up to the 1000 mg/kg/day dose group.

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

Examinations

Parental animals: Observations and examinations
CAGE SIDE OBSERVATIONS: Yes
- Time schedule:
Males and females (main study groups): 2 times/day (before administration, 61-189 minutes after administration) during the administration period. Once a day during the recovery period.
Females (mating study groups): 2 times/day (before administration, 60-211 minutes after administrat ion) during the administration period.
DETAILED CLINICAL OBSERVATIONS: Yes
- Time schedule:
Males and females (main study groups): on day of grouping, on days 7, 14, 21 and 27 of administra tion period.
Females (mating study groups): on day of grouping, on days 7 and 14 of administration period, on days 1, 8 and 15 of gestation period, on day 4 of lactation period.

BODY WEIGHT: Yes
- Time schedule for examinations:
Males and females (main study groups):
Twice a week (On days 1, 4, 8, 11, 15, 18, 22, 25, 28 and 29 of administration period, on days 1, 4, 8, 11, 14 and 15 of recovery period).
Females (mating study groups): Twice a week (On days 1, 4, 8, 11, 15 and 18 of administration period, on days 0, 7, 14 and 20 of gestation period, on days 0, 4 and 5 of lactation period).

FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):
- Food consumption: Yes
- Time schedule for examinations:
Males and females (main study groups):
Twice a week (Males: On days 2, 5, 9 and 12 of administration period, on days 2, 5, 9 and 12 of rec overy period; Females: On days 2, 5, 9, 12, 16, 19, 23 and 26 of administration period, on days 2, 5, 9 and 12 of recovery period).

Females (mating study groups): Twice a week (On days 2, 5, 9 and 12 of administration period, on d ays 2, 9, 16 and 20 of gestation period, on days 2 of lactation period).

WATER INTAKE: Yes
- Time schedule for examinations:
Males and females (main study groups):
Twice a week (Males: On days 2, 5, 9 and 12 of administration period, on days 2, 5, 9 and 12 of recovery period; Females: On days 2, 5, 9, 12, 16, 19, 23 and 26 of administration period, on days 2, 5, 9 and 12 of recovery period).
Females (mating study groups): Twice a week (On days 2, 5, 9 and 12 of administration period, on days 2, 9, 16 and 20 of gestation period, on days 2 of lactation period).

OPHTHALMOSCOPIC EXAMINATION: No
HAEMATOLOGY: Yes
- Time schedule for collection of blood:
Males and females (main study groups): At the end of administration period, or at the end of recovery period in both sexes
- Anaesthetic used for blood collection: Pentobarbital sodium
- Animals fasted: Yes
- How many animals:
At the end of administration period: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0, 62.5, 250, 1000 mg/kg bw/day)
At the end of recovery period: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0 and 1000 mg/kg bw/day)
- Parameters examined: red blood cell count, hemoglobin, hematocrit, mean corpuscular volu me, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, reticulocyte p ercentage, platelet count, white blood cell count, differential white blood cell count, prothrombin time, activated partial thromboplastin time, fibrinogen.

CLINICAL CHEMISTRY: Yes
- Time schedule for collection of blood:
Males and females (main study groups): 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: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0, 62.5, 250, 1000 mg/kg bw/day)
At the end of recovery period: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0 and 1000 mg/kg bw/day)
- Parameters checked: ALP, total cholesterol, triglyceride, total bilirubin, glucose, urea nitrogen, creati nine, sodium, potassium, chloride, calcium, inorganic phosphorus, total protein, albumin, A/G ratio, AST, ALT, γ-GT

URINALYSIS: Yes
- Time schedule for collection of urine:
Males and females (main study groups): Before the end of the administration period (day 23 of a dministration period) and before the end of recovery (days 12 of recovery period).
- Metabolism cages used for collection of urine: Yes
A urine collector to collect fresh urine samples under fasting but ad libitum drinking conditions, follo wed by collection of 24-hour urine samples under ad libitum feeding and drinking conditions.
- How many animals:
At the end of administration period: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0, 62.5, 250, 1000 mg/kg bw/day)
At the end of recovery period: 6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0 and 1000 mg/kg bw/day)
- Parameters checked:
Fresh urine: Color, pH, protein, glucose, ketones, bilirubin, occult blood, urobilinogen, sediment
24-urine: Specific gravity, urine volume (24-hour volume)

BLOOD HORMONE: Yes
- Time schedule for collection of serum:
Males and females (main study groups): At the end of administration period in both sexes
- Animals fasted: Yes
- How many animals:
6 males/dose (0, 62.5, 250, 1000 mg/kg bw/day), 5 females/dose (0, 62.5, 250, 1000 mg/kg bw/day)
- Parameters checked: Triiodothyronine (T3), Thyroxin (T4), and thyroid stimulating hormone (TSH)

NEUROBEHAVIOURAL EXAMINATION: Yes
- Time schedule for examinations:
Males and females (main study groups): Final week of administration (Manipulative test and meas urement of grip strength: Day 27 of administration, measurement of motor activity: Day 26 of adminis tration)
- Dose groups that were examined: Autopsy animals after the end of the administration period
- Battery of functions tested:
1) Manipulative Test. Pupillary reflex, approaching behavior, response to touch, auditory reflex, pain reflex
2) Measurement of Grip Strength. Following manipulative test, grip strength of forelimb and hind limb were measured by CPU gauge (San Diego Instruments Inc.).
3) Measurement of Spontaneous Motor Activity. Spontaneous motor activity (Ambulatory and vertical counts) was measured by Activity Monitor (MED Associates Inc.).
The measurements were collected at 10-minute intervals from 1 hour to 2 hours after administration.

Oestrous cyclicity (parental animals)
Vaginal smears were collected from all females in the mating study groups and microscopically examined every day from the day after the start of administration until the day copulation was c onfirmed.

Sperm parameters (parental animals)
Parameters examined in all P male parental generations: testis, epididymis and seminal vesicle weigh t, histopathological examinations for testes, epididymides, seminal vesicle and ventral prostate.

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 pentobarbital sodium anesthesia.
SACRIFICE: Males and females (main study groups): On next day after the last administration, Maternal animals: on Day 5 of lactation, and males and females recovery group: on Day 14 of recovery .
GROSS PATHOLOGY: Yes
ORGAN WEIGHT: Yes [main study groups: brain, pituitary, salivary glands, thyroids, adrenal gland, thymus, spleen, heart, liver, kidney, testes, epididymides, ventral prostate, seminal vesicles, ovaries, uterus; females in mating group: ovary, uterus]
HISTOPATHOLOGY: Yes, [main study groups: heart, lung, trachea, liver, pancreas, sublingual gland , submandibular gland, esophagus, stomach, duodenum, jejunum, ileum (including Peyer's patch), cecum, colon, rectum, thymus, spleen, mandibular lymph nodes, mesenteric lymph nodes, kidney, urinary bladder, testis, epididymis, ventral prostate, seminal vesicles (including coagulating gland), ovaries, uterus, vagina, pituitary, adrenal glands, thyroid (including parathyroid), cerebrum, cerebellum, pons, spinal cord, sciatic nerve, eye ball, Harderian gland, sternum and femur (including bone marrow s), muscle (rectus femoris), mammary gland; females in mating group: ovaries, uterus, vagina]

Postmortem examinations (offspring)
SACRIFICE
- The F1 offsprings were euthanized on PND4 by exsanguination under 20%Isoflurane 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 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 Steel method. For comparison of quantitative data be tween two groups in the recovery test, homogeneity of variance was analyzed by F-test. Then, if homo genous, student's t-test was applied. If not homogenous, Aspin-Welch's t-test was used.
Regarding clinical observation (except for frequency of urination, defecation, rearing and grooming) and sensory reactivity, Steel test was applied. Regarding implantation index, delivery index, birth index, live birth index, viability index, sex ratio and external abnormalities, Steel test was applied. Regarding copulation, fertility index, and gestation index, Fisher's test was applied.

Reproductive indices
Each parameter was determined by the following equations:
Copulation index (%) = (No. of pairs with successful copulation / No. of pairs) × 100
Fertility index (%) = (No. of pregnant females / No. of pairs with successful copulation) × 100
Gestation index (%) = (No. of dams having live pups / No. of pregnant dams) × 100
Length of gestation (days)
Implantation index (%) = (No. of implantation scars / No. of corpora lutea) × 100
Delivery index (%) = (No. of pups born / No. of implantation scars) × 100
Birth index (%) = (No. of live pups born / No. of implantation scars) × 100
Live birth index (%) = (No. of live pups born / No. of pups born) × 100
Sex ratio on Day 4 of lactation = No. of male pups / No. of female pups
External abnormalities (%) = (No. of pups with external abnormalities / No. of live pups) × 100

Offspring viability indices
Viability index (%) = (No. of live pups on Day 4 of lactation/ No. of live pups born) × 100

Results and discussion

Results: P0 (first parental generation)

General toxicity (P0)

Clinical signs
no effects observed

Mortality
no mortality observed

Body weight and weight changes
no effects observed

Food consumption and compound intake (if feeding study)
no effects observed

Food efficiency
not examined

Water consumption and compound intake (if drinking water study)
no effects observed

Ophthalmological findings
not examined

Haematological findings
effects observed, treatment-related

Description (incidence and severity)
See 7.5.1 Repeated dose toxicity.001

Clinical biochemistry findings
no effects observed

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)
See 7.5.1 Repeated dose toxicity.001

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 1000 mg/kg bw/day.

Effect levels (P0)

Key result
false

Dose descriptor
NOAEL

Effect level

1000 mg/kg bw/day (actual dose received)

Based on
test mat.

Sex
male

Basis for effect level
other:
No toxic effects were observed in males up to the highest dose of 1000 mg/kg bw/day.

Key result
false

Dose descriptor
NOAEL

Effect level

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

Based on
test mat.

Sex
female

Basis for effect level
haematology
Decreases in hematocrit and hemoglobin were observed in females at 1000 mg/kg bw/day.
organ weights and organ / body weight ratios
Increase in absolute and relative liver weights, increase in absolute adrenal weight and increase te ndency in relative adrenal weight were observed in females at 1000 mg/kg bw/day.

Key result
false

Dose descriptor
NOAEL

Effect level

1000 mg/kg bw/day (actual dose received)

Based on
test mat.

Sex
male/female

Basis for effect level
reproductive performance
No reproductive effects were observed in both males and females up to 1000 mg/kg bw/day.

Results: F1 generation

General toxicity (F1)

Clinical signs
no effects observed

Mortality / viability
no mortality observed

Body weight and weight changes
effects observed, treatment-related

Gross pathological findings
no effects observed

Details on results (F1)

F1 offspring in the 1000 mg/kg bw/day group showed a tendency to lower body weight or lower body weight on lactation day 0.

Effect levels (F1)

Key result
false

Dose descriptor
NOAEL

Generation
F1

Effect level

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

Based on
test mat.

Sex
male/female

Basis for effect level
body weight and weight gain
F1 offspring in the 1000 mg/kg bw/day group showed a tendency to lower body weight or lower body weight on lactation day 0.

Overall reproductive toxicity

Key result
false

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/PDF9005-70-3d.pdf

Applicant's summary and conclusion

Conclusions
In the combined repeated oral dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) described above, low body weights of pups on lactation day 0 were observed at maternally toxic doses. The NOAEL for reproductive toxicity of polyoxyethylenesorbitan fatty acid(C12-18)ester was regarded to be 1000 mg/kg bw/day because no reproductive toxic effects were observed.
The NOAEL for developmental toxicity of polyoxyethylenesorbitan fatty acid(C12-18)ester was regarded to be 250 mg/kg bw/day because of a trend towards lower or lower body weights in F1 pups at 1000 mg/kg bw/day.

DOMAIN

SUBSTANCE: Polyoxyethylenesorbitan fatty acid(C12-18)ester

UUID: c8355b50-875d-42c8-a5d3-3094f20b1fde
Dossier UUID:
Author:
Date: 2022-03-25T15:25:46.000+09:00
Remarks:

Substance name
Polyoxyethylenesorbitan fatty acid(C12-18)ester

Legal entity
National Institute of Health Sciences / Kawasaki / Japan

Identification of substance

Reference substance
Polyoxyethylenesorbitan fatty acid(C12-18)ester / 9005-70-3 / 618-422-4

EC number	EC name
618-422-4	EC Inventory
CAS number	**CAS name**
9005-70-3	
IUPAC name	

Role in the supply chain

Manufacturer
false

Importer
false

Only representative
false

Downstream user
false

References

Reference Substances

REFERENCE_SUBSTANCE: Polyoxyethylenesorbitan fatty acid(C12-18)ester

UUID: 9152eb94-d1f7-4d0a-ac90-0470dcfc2f34
Dossier UUID:
Author:
Date: 2022-03-25T14:42:39.000+09:00
Remarks:

Reference substance name
Polyoxyethylenesorbitan fatty acid(C12-18)ester

Inventory

Inventory number

Inventory name

Inventory
EC Inventory

Inventory number
618-422-4

CAS number

Molecular formula

Description

CAS number
9005-70-3

Synonyms

Synonyms

Identifier
other:

Identity
polyoxyethylene sorbitan trioleate

Identifier
other:

Identity
Tween 85

Molecular and structural information

Molecular formula
C60H108O8(C2H4O)20

Molecular weight

1838.5

Test Materials

TEST_MATERIAL_INFORMATION: Polyoxyethylenesorbitan fatty acid(C12-18)ester

UUID:	dc6c1a49-b20f-4b3b-b187-a4d631c1e214
Dossier UUID:	
Author:	
Date:	2022-03-25T14:49:31.000+09:00
Remarks:	

Name
Polyoxyethylenesorbitan fatty acid(C12-18)ester

Composition

Other characteristics

Test material form
liquid: viscous

Details on test material
CAS No.: 9005-70-3

Literatures

LITERATURE: Combined repeated dose toxicity study with the reproductive/developmental toxicity screening test of polyoxyethylene sorbitan trioleate by oral administration in rats

UUID: 74c15b50-0eb8-4ad3-bc6f-5bf480e3c3a6
Dossier UUID:
Author:
Date: 2021-10-18T14:53:15.000+09:00
Remarks:

General information

Reference Type
study report

Title
Combined repeated dose toxicity study with the reproductive/developmental toxicity screening test of polyoxyethylene sorbitan trioleate 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/PDF9005-70-3d.pdf

Testing facility
Nihon Bioresearch Inc.

Report number
100230

LITERATURE: In Vitro Chromosomal Aberration Test of Polyoxyethylene sorbitan trioleate on Cultured Chinese Hamster Cells.

UUID: 62452636-5f6e-49ef-bd68-199fbb3700af
Dossier UUID:
Author:
Date: 2022-03-03T17:07:07.000+09:00
Remarks:

General information

Reference Type
study report

Title
In Vitro Chromosomal Aberration Test of Polyoxyethylene sorbitan trioleate on 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/PDF9005-70-3f.pdf

Testing facility
Nihon Bioresearch Inc.

Report date
2011-03-29

Report number
970630

LITERATURE: Reverse Mutation Test of Polyoxyethylene sorbitan trioleate on Bacteria.

UUID: 4d39dcfb-06cf-42d1-85cb-db5ff4a3cfe0
Dossier UUID:
Author:
Date: 2022-03-01T15:15:07.000+09:00
Remarks:

General information

Reference Type
study report

Title
Reverse Mutation Test of Polyoxyethylene sorbitan trioleate 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/PDF9005-70-3e.pdf

Testing facility
Nihon Bioresearch Inc.

Report date
2011-03-29

Report number
900930