Name: OECD_SIDS / SUBSTANCE : 2-Decyltetradecanol / 2-decyltetradecan-1-ol / 58670-89-6 Fri, 29 Nov 2024, 09:50:48+0900 /

Printing date: 2024-11-29T09:50:48.800+09:00

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DOSSIER:

UUID: 0
Dossier UUID:
Author:
Date: 2024-11-29T09:50:48.580+09:00
Remarks:

Dossier header

Dossier submission type

Name
OECD SIDS

Version
core 9.0

Name (given by user)

Dossier subject

Dossier subject
2-Decyltetradecanol / 2-decyltetradecan-1-ol / 58670-89-6

Public name

Submitting legal entity
National Institute of Health Sciences

Dossier creation date/time
Fri, 29 Nov 2024, 09:50:48+0900

Used in category

LEGAL_ENTITY: National Institute of Health Sciences

UUID:	71368d76-19ad-4a2e-bc26-6c8ef515e6e3
Dossier UUID:	
Author:	
Date:	2024-05-29T16:58:20.759+09:00
Remarks:	

General information

Legal entity name
National Institute of Health Sciences

2-Decyltetradecanol

General information

Identification

SUBSTANCE: 2-Decyltetradecanol

UUID:	bf62d2a6-6ee6-48ef-9dcf-31264ba2fbf9
Dossier UUID:	
Author:	
Date:	2023-01-13T10:45:47.000+09:00
Remarks:	

Substance name
2-Decyltetradecanol

Identification of substance

Reference substance
2-decyltetradecanol / 2-decyltetradecan-1-ol / 58670-89-6 / 261-385-0

EC number	**EC name**
261-385-0	EC Inventory
CAS number	**CAS name**
58670-89-6	
IUPAC name	
2-decyltetradecan-1-ol	

Role in the supply chain

Manufacturer
false

Importer
false

Only representative
false

Downstream user
false

Toxicological information

Repeated dose toxicity

Repeated dose toxicity: oral

ENDPOINT_STUDY_RECORD: Repeated dose toxicity: oral. 001

UUID:	edff7289-2be1-496f-824c-f0ccc2470453
Dossier UUID:	
Author:	
Date:	2023-01-13T10:41:07.000+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
Reliability 1

Cross-reference

Reason / purpose for cross-reference
reference to same study

Related information
OECD / Toxicity to reproduction / Toxicity to reproduction. 001 / 2-Decyltetradecanol / 2-decyltetradecan-1-ol / 58670-89-6

Data source

Reference

Combined repeat dose and reproductive/developmental toxicity screening test of 2-decyltetradecanol o / Ministry of Health, Labour and Welfare (MHLW), Japan / study report

Data access
data published https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF58670-89-6d.pdf

Materials and methods

Test guideline

Qualifier
according to guideline

Guideline
other: Guideline for Combined Repeated Dose Toxicity Study with the Reproduction /Developmental Toxicity Screening Test in Mammalian Species (Chemical Substances Control Law of Japan)

Version / remarks
similar to OECD TG422

GLP compliance
yes

Limit test
no

Test material

Test material information
2-Decyltetradecanol

Specific details on test material used for the study
-Name of test material (as cited in study report): 2-Decyltetradecanol
- Analytical purity: 98.4%
- Storage condition of test material: Seald and refrigerated (actual temperature: 3-8°C)
- Stability under test conditions: The stability of test material was identified by analysis of the rem ainder.

Test animals

Species
rat
common rodent species

Strain
other: Crl: CD (SD)

Sex
male/female

Details on test animals or test system and environmental conditions
TEST ANIMALS
- Source: Charles River Japan, Inc., Atsugi Breeding Center.
- Age at study initiation: 10 weeks old
- Weight at study initiation: Male: 342.9-448.9 g, Female: 206.9-281.0 g
- Housing: Animals were individually housed in bracket-type metallic wire-mesh cages (220W × 270D× 190H mm), from gestation day 18 to lactation day 4, Dams were bred individually or with individual littermates in plastic cages (350W x 400D x 180H mm) and bedding.
- Diet: Solid feed (CE-2: CLEA Japan Inc.) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation period: 15 days

ENVIRONMENTAL CONDITIONS
- Temperature (°C): 21.0-25.0 (actual temperature: 22.0-25.5°C)
- Humidity (%): 40.0-75.0% (actual humidity: 46.0-66.0%)
- Air changes (per hr): 15
- Photoperiod (hrs dark / hrs light): 12 hr dark/12 hr light (light: 7:00-19:00)

Administration / exposure

Route of administration
oral: gavage

Vehicle
corn oil

Details on oral exposure
- Amount of vehicle (if gavage): 4 mL/kg
- Dosing volume: 4 mL/kg

Analytical verification of doses or concentrations
yes

Details on analytical verification of doses or concentrations
The concentrations of each test suspension used at day1 of administration were analyzed by HPLC. The results showed that the concentration of each test suspension was 98.9 to 101.3% of the nominal concentration.

Duration of treatment / exposure
Males: 42 days including 14 days pre-mating
Females (mating group): 41-55 days including 14 days pre-mating, mating and gestation periods and the days until day 4 of lactation
Female (non-mating, satellite group): 42 days

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
Mating group: 12 animals/sex /dose (0, 62.5, 250, and 1000 mg/kg bw/day).

Non-mating group (Satellite group): 10 females/dose (0 and 1000 mg/kg bw/day).
Recovery group: 5 males/dose in the mating group (0 and 1000 mg/kg bw/day) and 5 females/dose in the non-mating groups (0 and 1000 mg/kg bw/day)

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 test guideline (Chemical Substances Control Law of Japan) and the6 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, 100, 300 or 1,000 mg/kg bw/day. No treatment-related effects on clinical signs, body weight, haematology, blood chemistry, or pathology were observed up to the highest dose of 1000 mg/kg bw/day in both sexes.
- Rationale for animal assignment (if not random): Body weight-balanced randomization

Examinations

Observations and examinations performed and frequency
CAGE SIDE OBSERVATIONS: Yes
- Time schedule: 2 times/day (before administration, after administration) during the administration period. Once a day during the recovery period.

DETAILED CLINICAL OBSERVATIONS: Yes
- Time schedule:
Males: At the end of acclimation period, Days 8, 15, 24, 30, 36, and 42 of administration and Days 7 and 14 of recovery period.
Females in the mating groups: At the end of acclimation period, Days 8, 15, 24, 30, 36, and 42 of administration period, once during lactation period (lactation day 0 from day 4) for delivered females and Day 49 for not delivered females until Day 49.
Females in the non-mating groups (satellite group): At the end of acclimation period, Days 8, 15, 24, 30, 36, and 42 of administration and Days 7 and 14 of recovery period.

BODY WEIGHT: Yes
- Time schedule for examinations:
Males: Days 1, 4, 7, 14, 21, 28, 35, and 42 of administration period and on the day of necropsy, and Days 1, 7 and 14 of recovery period and on the day of necropsy.
Females in the mating groups: Days 1, 4, 7, and 14 of administration period, Days 0, 7, 14, and 20 of gestation, Days 0, 4 of lactation, and on the day of necropsy.
Females in the non-mating groups (satellite group): Days 1, 4, 7, 14, 21, 28, 35, and 42 of administration period and on the day of necropsy, and Days 1, 7 and 14 of recovery period and on the day of necropsy.

Food consumption: Yes
Measurement of food consumption was conducted on all animals at the following frequencies:
Males: Days 1-2, 7-8, 14-15, 29-30, 35-36 and 41-42 of administration period. Days 6-7 and 12-13 of recovery period.
Females in the mating groups: Days 1-2, 7-8 and 14-15 of administration period. Days 0-1, 7-8, 14-15, and 20-21 of gestation period. Days 3-4 of lactation period. Days 29-30, 35-36, 41-42 and 48-49 of administration period for unmated females.
Females in the non-mating groups (satellite group): Days 1-2, 7-8, 14-15, 21-22, 29-30, 35-36 and 41-42 of administration period. Days 6-7 and 12-13 of recovery period.

OPHTHALMOSCOPIC EXAMINATION: No

HAEMATOLOGY: Yes
- Time schedule for collection of blood: At the end of administration period, or at the end of recovery period in both sexes
- Anaesthetic used for blood collection: Pentbarbital sodium
- Animals fasted: Yes
- How many animals:
5 animals/sex/group
- Parameters examined: Red blood cell count, hemoglobin, hematocrit, mean corpuscular volume , mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, reticulocyte per centage, platelet count, white blood cell count, differential white blood cell count, prothrombin time, activated partial thromboplastin time.

CLINICAL CHEMISTRY: Yes
- Time schedule for collection of blood: At the end of administration period, or at the end of recovery period in both sexes
- Animals fasted: Yes
- How many animals:
5 animals/sex/group
- Parameters checked: ALP, total cholesterol, triglyceride, phospholipids, total bilirubin, glucose, bloo d urea nitrogen, creatinine, sodium, potassium, chloride, calcium, inorganic phosphorus, total protein, albumin, A/G ratio, AST, ALT, LDH, γ-GTP, bile acid.

BLOOD HORMONE: No

URINALYSIS OF MALES: Yes
- Time schedule for collection of urine: On the final week of administration (Day 37 of administration) and on the final week of recovery (Day 13 of recovery)
- Metabolism cages used for collection of urine: Yes
- How many animals: 5 animals/group
- Parameters checked: pH, protein, ketones, glucose, occult blood, bilirubin, urobilinogen, color, s ediment, osmotic pressure, sodium, potassium, chloride, urine volume (24-hour volume)

NEUROBEHAVIOURAL (FUNCTIONAL) EXAMINATION: Yes
- Time schedule for examinations:
Males: On the final week of administration (Manipulative Test: Day 42, Measurement of Grip Strength and Motor Activity: Day 39). No examinations were performed during the recovery period
Females in the mating groups: Day 5 of lactation
Females in the non-mating groups (satellite group): On the final week of administration (Manipulative Test: Day 42, Measurement of Grip Strength and Motor Activity: Day 41). No examinations were p erformed during the recovery period.
- Dose groups that were examined: All dose groups (5 animals/sex/group)
- Battery of functions tested:
1) Manipulative Test. Prayer's reaction, pupillary reflex, visual placing, startle reaction, withdrawal reflex, eyelid reflex, and righting reflex
2) Measurement of Grip Strength. Grip strength of forelimb and hind limb were measured by grip strength meter.
3) Measurement of Motor Activity. Motor activity was measured by a motor activity sensor for experimental animals SUPER-MEX (Muromachi Kikai. Co., Ltd.). The measurement was conducted for 20 min.

Sacrifice and pathology
GROSS PATHOLOGY: Yes
ORGAN WEIGHT: Yes [brain, thyroids (including parathyroids), thymus, heart, liver, kidney, spleen, adrenal gland, testis, epididymis, prostate, seminal vesicles, ovary, uterus]
HISTOPATHOLOGY: Yes, [brain, spinal cord, pituitary, eyeball (Harderian gland), submandibular gland, sublingual gland, trachea, thyroid, parathyroid, thymus, heart, lung (including bronchial), liver, kidney,

spleen, pancreas, adrenal gland, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, subm andibular lymph node, mesenteric lymph node, testis, epididymis, prostate, seminal vesicles, ovary, uterus, vagina, bladder, femur (including bone marrows), skeletal muscle, sciatic nerve, mammary gla nd, and gross abnormalities site.

Statistics
Changes in estrous cyclicity, copulation index and fertility index were analyzed by Fisher's test. G raded pathological data was analyzed by Mann-Whitney's U test (significance level = 0.05) and pathol ogical data with number of positive and negative animals was analyzed by one-sided Fisher's test. Ot her data obtained values in each animal or mean of a litter was one data, and these data were compar ed among the satellite groups and other among the groups. These data were analyzed using F-test for homogeneity of distribution. The Student's t-test and the Aspin-Welch's t-test were conducted for homogenous and non-homogenous distribution, respectively to compare the control and individu al treatment groups. Three or more groups setting, these data were analyzed using Bartlett's test for homogeneity of distribution. The Dunnett's multiple comparison test after the ANOVA and the Dunnett's-type mean rank sum test after Kruskal-Wallis's H test were conducted for homogenous an d non-homogenous distribution, respectively to compare the control and individual treatment groups. Significance level was set at 0.05 compared with the control group and among the groups.

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)
not examined

Ophthalmological findings
not examined

Haematological findings
effects observed, treatment-related

Description (incidence and severity)
[At the end of dosing period]:
A significant prolongation of PT and a trend toward prolongation of APTT were observed in males at 250 mg/kg bw/day and above.
[At the end of recovery period]:
In males at 1000 mg/kg bw/day, PT tended to be prolonged, and APTT was significantly prolonged.

Clinical biochemistry findings
effects observed, treatment-related

Description (incidence and severity)
[At the end of dosing period]:

A significant increase in LDH was observed in males at 250 mg/kg bw/day and above.
[At the end of recovery period]:
There were no changes related to the test substance in any groups.

Urinalysis findings
effects observed, treatment-related

Description (incidence and severity)
[At the dosing period]:
A positive occult blood reaction (2 +) was observed in 1 male at 1000 mg/kg bw/day. Significant decreases in urine volume, sodium, potassium, and chloride excretion were observed in non-mated females at 1000 mg/kg bw/day.
[At the recovery period]:
There were no changes related to the test substance in any groups.

Behaviour (functional findings)
no effects observed

Immunological findings
not examined

Organ weight findings including organ / body weight ratios
no effects observed

Gross pathological findings
no effects observed

Neuropathological findings
not examined

Histopathological findings: non-neoplastic
no effects observed

Histopathological findings: neoplastic
not examined

Effect levels

Key result
true

Dose descriptor
NOAEL

Effect level

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

Based on
test mat.

Sex
male

Basis for effect level
clinical biochemistry
A significant increase in LDH was observed in males at 250 mg/kg bw/day and above.

haematology
A significant prolongation of PT and a trend toward prolongation of APTT were observed in males at 250 mg/kg bw/day and above.

Key result
true

Dose descriptor
NOAEL

Effect level

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

Based on
test mat.

Sex
female

Basis for effect level
urinalysis
Significant decreases in urine volume, sodium, potassium, and chloride excretion were observed in non-mated 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/PDF58670-89-6d.pdf

Applicant's summary and conclusion

Conclusions
The NOAEL for repeated dose toxicity in this study was determined to be 65 and 250 mg/kg bw/day for males and females, respectively.

Executive summary

A combined repeated oral dose toxicity study with the reproduction/developmental toxicity screening test was performed according to a Japanese guideline (similar to OECD TG 422).

SD rats were treated orally with 2-decyltetradecanol at the doses of 0, 65, 250 and 1000 mg/kg bw/day. Males (12 males/dose, of which 5 males/dose were assigned to the recovery group) were dosed for 42 days including a 14-day pre-mating period. Females (12 females/dose) were dosed for 41-55 days including 14-day premating, mating, and gestation periods and days until day 4 of lactation. In addition, as a satellite group, females (10 females/dose, of which 5 males/dose were assigned to the recovery group) received 0 and 1000 mg/kg bw/day for 42 days without mating.

The following findings were observed in the examination during the administration period or at the end of administration period. In the urinalysis, a positive occult blood reaction (2 +) was observed in 1 male at 1000 mg/kg bw/day. Significant decreases in urine volume, sodium, potassium, and chloride excretion were observed in non-mated females at 1000 mg/kg bw/day. In the haematology, a significant prolongation of PT and a trend toward prolongation of APTT were observed in males at 250 mg/kg bw/day and above. In the clinical chemistry, a significant increase in LDH was observed in males at 250 mg/kg bw/day and above. At the end of the recovery period, APTT was significantly prolonged, PT tended to

be prolonged, and LDH tended to increase in males at 1000 mg/kg bw/day. However, it was a reversible change because the degree was reduced.

Based on the above results, NOAEL for the repeated dose toxicity of 2-decyltetradecanol was determined to be 65 and 250 mg/kg bw/day for males and females, respectively.

Genetic toxicity

Genetic toxicity in vitro

ENDPOINT_STUDY_RECORD: Genetic toxicity in vitro.001

UUID:	c9f6a730-c475-494b-b906-66c4c2901eb7
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Remarks:	

Administrative data

Endpoint
in vitro gene mutation study in bacteria

Type of information
experimental 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

Reverse Mutation Test of 2-Decyltetradecanol 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
JAPAN: Guidelines for Screening Mutagenicity Testing Of Chemicals

genetic toxicity in vitro, other

Version / remarks
Simiral to OECD TG 471 (Bacterial Reverse Mutation Assay)

Deviations
no

GLP compliance
yes (incl. QA statement)

Test material

Test material information
2-Decyltetradecanol

Specific details on test material used for the study
-Name of test material (as cited in study report): 2-Decyltetradecanol
- Analytical purity: 98.4%
- Storage condition of test material: Seald and refrigerated (actual temperature: 3-7°C)
- Stability under test conditions: The stability of test material was identified by analysis of the rem ainder.

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:
313, 625, 1250, 2500, 5000 µg/plate (TA100, TA1535, TA98, TA537 and WP2uvrA strains)
+S9 mix:
313, 625, 1250, 2500, 5000 µg/plate (TA100, TA1535, TA98, TA537 and WP2uvrA strains)

Maximum concentration was established based on the result of the preliminary test at concentration up to 5000 ug/plate. In this test, no growth inhibition was observed for all strains with and without S9 mix.

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

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) (TA100, WP2uvrA, TA98), Sodium azide (SAZ) (TA1535) and 9-Aminoacridine (9 AA) (TA1537)
+S9 mix: 2-Aminoanthracene (2AA) (TA1535, WP2uvrA), Benzo[a]pyrene (B[a]P) (TA100, TA98, TA1537)

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: 2
NUMBER OF REPLICATIONS: 2
DETERMINATION OF CYTOTOXICITY
- Method: other: growth inhibition

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

Statistics
no

Results and discussion

Test results

Key result
false

Species / strain
S. typhimurium TA 1535
bacteria

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity / choice of top concentrations
no cytotoxicity

Vehicle controls validity
valid

Untreated negative controls validity
not examined

True negative controls validity
not examined

Positive controls validity
valid

Key result
false

Species / strain
S. typhimurium TA 1537
bacteria

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity / choice of top concentrations
no cytotoxicity

Vehicle controls validity
valid

Untreated negative controls validity
not examined

True negative controls validity
not examined

Positive controls validity
valid

Key result
false

Species / strain
S. typhimurium TA 98
bacteria

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity / choice of top concentrations
no cytotoxicity

Vehicle controls validity
valid

Untreated negative controls validity
not examined

True negative controls validity
not examined

Positive controls validity
valid

Key result
false

Species / strain
S. typhimurium TA 100
bacteria

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity / choice of top concentrations
no cytotoxicity

Vehicle controls validity
valid

Untreated negative controls validity
not examined

True negative controls validity
not examined

Positive controls validity
valid

Key result
false

Species / strain
E. coli WP2 uvr A
bacteria

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity / choice of top concentrations
no cytotoxicity

Vehicle controls validity
valid

Untreated negative controls validity
not examined

True negative controls validity
not examined

Positive controls validity
valid

Any other information on results incl. tables

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

https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF58670-89-6e.pdf

Please also see the attached files (Tables in English)

Overall remarks, attachments

Attachments

Attached (sanitised) documents for publication
58670-89-6_Ames Tables.xlsx / 21.773 KB (application/vnd.openxmlformats-officedocument.spreadsheetml.sheet)

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, 2-decyltetradecanol was negative with or without metabolic activation.

ENDPOINT_STUDY_RECORD: Genetic toxicity in vitro.002

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Remarks:	

Administrative data

Endpoint
in vitro chromosome aberration study in mammalian cells

Type of information
experimental study

Adequacy of study
key study

Robust study summary
false

Used for classification
false

Used for SDS
false

Reliability
1 (reliable without restriction)

Rationale for reliability incl. deficiencies
guideline study
Reliability 1

Data source

Reference

In Vitro Chromosomal Aberration Test of 2-Decyltetradecanol on Cultured Chinese Hamster Cells. / Ministry of Health, Labour and Welfare (MHLW), Japan / study report

Data access
data published

Materials and methods

Test guideline

Qualifier
according to guideline

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

Version / remarks
Simiral to OECD TG 473 (In Vitro Mammalian Chromosomal Aberration Test)

Deviations
no

GLP compliance
yes

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

Test material

Test material information
2-Decyltetradecanol

Specific details on test material used for the study
-Name of test material (as cited in study report): 2-Decyltetradecanol
- Analytical purity: 98.4%
- Storage condition of test material: Seald and refrigerated (actual temperature: 3-7°C)
- Stability under test conditions: The stability of test material was identified by analysis of the rem
ainder.

Method

Species / strain

Species / strain / cell type
Chinese hamster lung (CHL/IU)
mammalian cell line

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:
0.055, 0.11, 0.22, 0.44, 0.88, 1.8, 3.5 mg/mL

Main study:
-S9 (short-term treatment): 0.44, 0.88, 1.8, 3.5 mg/mL
+S9 (short-term treatment): 0.44, 0.88, 1.8, 3.5 mg/mL
-S9 (continuous treatment, 24hr): 0.044, 0.088, 1.8, 3.5 mg/mL

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

Controls

Untreated negative controls
no

Negative solvent / vehicle controls
yes

True negative controls
no

Positive controls
yes

Positive control substance
cyclophosphamide
+S9
mitomycin C
-S9

Details on test system and experimental conditions
METHOD OF APPLICATION:
Exposure duration:
- [short-term treatment]: 6 hrs + 18 hr,
- [continuous treatment]: 24 hrs
SPINDLE INHIBITOR: Colcemid
STAIN: Giemsa stain (3 v/v%) for 8 min.
NUMBER OF REPLICATIONS: 2
NUMBER OF CELLS EVALUATED: 100 + 100 cells /concentration
DETERMINATION OF CYTOTOXICITY
- Method: relative total growth

Evaluation criteria
The frequency of cells with structural chromosomal aberrations and polyploid cells was tested for si gnificance by Fisher's exact test (one-sided test, P<0.01) between the negative control and test sub stance treated groups. If a significant difference was observed, a Chochran-Armitage trend tests (on e-sided test, P<0.01) was performed for dose dependency. The results of these tests were used as a r eference for a comprehensive evaluation, taking into account biological considerations.

Statistics
Yes

Results and discussion

Test results

Key result
false

Species / strain
Chinese hamster lung (CHL/IU)
mammalian cell line

Metabolic activation
with and without

Genotoxicity
negative

Cytotoxicity / choice of top concentrations
no cytotoxicity

Vehicle controls validity
valid

Untreated negative controls validity
not examined

True negative controls validity
not examined

Positive controls validity
valid

Any other information on results incl. tables

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

https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF58670-89-6f.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, 2-decyltetradecanol was negative with or without metabolic activation.

Toxicity to reproduction

Toxicity to reproduction

ENDPOINT_STUDY_RECORD: Toxicity to reproduction. 001

UUID: 7bf79153-d395-4e39-878d-83435f7108e4
Dossier UUID:
Author:
Date: 2023-01-13T10:44:19.000+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
Reliability 1

Cross-reference

Reason / purpose for cross-reference
reference to same study

Related information
OECD / Repeated dose toxicity: oral / Repeated dose toxicity: oral. 001 / 2-Decyltetradecanol / 2-decyltetradecan-1-ol / 58670-89-6

Data source

Reference

Combined repeat dose and reproductive/developmental toxicity screening test of 2-decyltetradecanol o / Ministry of Health, Labour and Welfare (MHLW), Japan / study report

Data access
data published https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF58670-89-6d.pdf

Materials and methods

Test guideline

Qualifier
according to guideline

Guideline
other: Guideline for Combined Repeated Dose Toxicity Study with the Reproduction /Developmental Toxicity Screening Test in Mammalian Species (Chemical Substances Control Law of Japan)

Version / remarks
Simiral to OECD TG422

GLP compliance
yes

Limit test
no

Test material

Test material information
2-Decyltetradecanol

Specific details on test material used for the study
-Name of test material (as cited in study report): 2-Decyltetradecanol
- Analytical purity: 98.4%
- Storage condition of test material: Seald and refrigerated (actual temperature: 3-8°C)
- Stability under test conditions: The stability of test material was identified by analysis of the rem ainder.

Test animals

Species
rat

Strain
other: Crl: CD (SD)

Sex
male/female

Details on test animals or test system and environmental conditions
TEST ANIMALS
- Source: Charles River Japan, Inc., Atsugi Breeding Center.
- Age at study initiation: 10 weeks old
- Weight at study initiation: Male: 342.9-448.9 g, Female: 206.9-281.0 g
- Housing: Animals were individually housed in bracket-type metallic wire-mesh cages (220W × 270D× 190H mm), from gestation day 18 to lactation day 4, Dams were bred individually or with individual littermates in plastic cages (350W x 400D x 180H mm) and bedding.
- Diet: Solid feed (CE-2: CLEA Japan Inc.) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation period: 15 days
ENVIRONMENTAL CONDITIONS
- Temperature (°C): 21.0-25.0 (actual temperature: 22.0-25.5°C)
- Humidity (%): 40.0-75.0% (actual humidity: 46.0-66.0%)
- Air changes (per hr): 15
- Photoperiod (hrs dark / hrs light): 12 hr dark/12 hr light (light: 7:00-19:00)

Administration / exposure

Route of administration
oral: gavage

Vehicle
corn oil

Details on exposure
- Amount of vehicle (if gavage): 4 mL/kg
- Dosing volume: 4 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 suspension used at day1 of administration were analyzed by HPLC. The results showed that the concentration of each test suspension was 98.9 to 101.3% of the nominal concentration.

Duration of treatment / exposure
Males: 42 days including 14 days pre-mating
Females (mating group): 41-55 days including 14 day5 pre-mating, mating and gestation periods and the days until day 4 of lactation
Female (non-mating, satellite group): 42 days

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
Mating group: 12 animals/sex /dose (0, 62.5, 250, and 1000 mg/kg bw/day).
Non-mating group (Satellite group): 10 females/dose (0 and 1000 mg/kg bw/day).
Recovery group: 5 males/dose in the mating group (0 and 1000 mg/kg bw/day) and 5 females/dose in the non-mating groups (0 and 1000 mg/kg bw/day)

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 test guideline (Chemical Substances Control Law of Japan) and the6 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, 100, 300 or 1,000 mg/kg bw/day. No treatment-related effects on clinical signs, body weight, haematology, blood chemistry, or pathology were observed up to the highest dose of 1000 mg/kg bw/day in both sexes.
- Rationale for animal assignment (if not random): Body weight-balanced randomization

Examinations

Parental animals: Observations and examinations
CAGE SIDE OBSERVATIONS: Yes
- Time schedule: 2 times/day (before administration, after administration) during the administration period. Once a day during the recovery period.

DETAILED CLINICAL OBSERVATIONS: Yes
- Time schedule:
Males: At the end of acclimation period, Days 8, 15, 24, 30, 36, and 42 of administration and Days 7 and 14 of recovery period.
Females in the mating groups: At the end of acclimation period, Days 8, 15, 24, 30, 36, and 42 of administration period, once during lactation period (lactation day 0 from day 4) for delivered females and Day 49 for not delivered females until Day 49.
Females in the non-mating groups (satellite group): At the end of acclimation period, Days 8, 15, 24, 30, 36, and 42 of administration and Days 7 and 14 of recovery period.

BODY WEIGHT: Yes
- Time schedule for examinations:
Males: Days 1, 4, 7, 14, 21, 28, 35, and 42 of administration period and on the day of necropsy, and Days 1, 7 and 14 of recovery period and on the day of necropsy.
Females in the mating groups: Days 1, 4, 7, and 14 of administration period, Days 0, 7, 14, and 20 of gestation, Days 0, 4 of lactation, and on the day of necropsy.
Females in the non-mating groups (satellite group): Days 1, 4, 7, 14, 21, 28, 35, and 42 of administration period and on the day of necropsy, and Days 1, 7 and 14 of recovery period and on the day of necropsy.

Food consumption: Yes
Measurement of food consumption was conducted on all animals at the following frequencies:
Males: Days 1-2, 7-8, 14-15, 29-30, 35-36 and 41-42 of administration period. Days 6-7 and 12-13 of recovery period.
Females in the mating groups: Days 1-2, 7-8 and 14-15 of administration period. Days 0-1, 7-8, 14-15, and 20-21 of gestation period. Days 3-4 of lactation period. Days 29-30, 35-36, 41-42 and 48-49 of administration period for unmated females.
Females in the non-mating groups (satellite group): Days 1-2, 7-8, 14-15, 21-22, 29-30, 35-36 and 41-42 of administration period. Days 6-7 and 12-13 of recovery period.

OPHTHALMOSCOPIC EXAMINATION: No

HAEMATOLOGY: Yes
- Time schedule for collection of blood: At the end of administration period, or at the end of recovery period in both sexes
- Anaesthetic used for blood collection: Pentbarbital sodium

- Animals fasted: Yes
- How many animals:
5 animals/sex/group
- Parameters examined: Red blood cell count, hemoglobin, hematocrit, mean corpuscular volume , mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, reticulocyte per centage, platelet count, white blood cell count, differential white blood cell count, prothrombin time, activated partial thromboplastin time.

CLINICAL CHEMISTRY: Yes
- Time schedule for collection of blood: At the end of administration period, or at the end of recovery period in both sexes
- Animals fasted: Yes
- How many animals:
5 animals/sex/group
- Parameters checked: ALP, total cholesterol, triglyceride, phospholipids, total bilirubin, glucose, bloo d urea nitrogen, creatinine, sodium, potassium, chloride, calcium, inorganic phosphorus, total protein, albumin, A/G ratio, AST, ALT, LDH, γ-GTP, bile acid.

BLOOD HORMONE: No

URINALYSIS OF MALES: Yes
- Time schedule for collection of urine: On the final week of administration (Day 37 of administration) and on the final week of recovery (Day 13 of recovery)
- Metabolism cages used for collection of urine: Yes
- How many animals: 5 animals/group
- Parameters checked: pH, protein, ketones, glucose, occult blood, bilirubin, urobilinogen, color, s ediment, osmotic pressure, sodium, potassium, chloride, urine volume (24-hour volume)

NEUROBEHAVIOURAL (FUNCTIONAL) EXAMINATION: Yes
- Time schedule for examinations:
Males: On the final week of administration (Manipulative Test: Day 42, Measurement of Grip Strength and Motor Activity: Day 39). No examinations were performed during the recovery period
Females in the mating groups: Day 5 of lactation
Females in the non-mating groups (satellite group): On the final week of administration (Manipulative Test: Day 42, Measurement of Grip Strength and Motor Activity: Day 41). No examinations were p erformed during the recovery period.
- Dose groups that were examined: All dose groups (5 animals/sex/group)
- Battery of functions tested:
1) Manipulative Test. Prayer's reaction, pupillary reflex, visual placing, startle reaction, withdrawal reflex, eyelid reflex, and righting reflex
2) Measurement of Grip Strength. Grip strength of forelimb and hind limb were measured by grip strength meter.
3) Measurement of Motor Activity. Motor activity was measured by a motor activity sensor for experimental animals SUPER-MEX (Muromachi Kikai. Co., Ltd.). The measurement was conducted for 20 min.

Oestrous cyclicity (parental animals)
Vaginal smears were collected from all females in the mating groups 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 all P male parental generations: testis weight, epididymis weight, histopatho logical 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 pentbarbital sodium anesthesia.
SACRIFICE: Males of mating groups and females of non-mating groups: On Day 43 (next day after the last administration), Maternal animals: on Day 5 of lactation period, and Males and females of r ecovery groups: on Day 15 of recovery period.

ORGAN WEIGHT: Yes [brain, thyroids (including parathyroids), thymus, heart, liver, kidney, spleen, adre nal gland, testis, epididymis, prostate, seminal vesicles, ovary, uterus]

HISTOPATHOLOGY: Yes, [brain, spinal cord, pituitary, eyeball (Harderian gland), submandibular gland, sublingual gland, trachea, thyroid, parathyroid, thymus, heart, lung (including bronchial), liver, kidney, spleen, pancreas, adrenal gland, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, submand ibular lymph node, mesenteric lymph node, testis, epididymis, prostate, seminal vesicles, ovary, uterus, vagina, bladder, femur (including bone marrows), skeletal muscle, sciatic nerve, mammary gland, and gross abnormalities site.

Postmortem examinations (offspring)
SACRIFICE
- The F1 offsprings were euthanized on PND4 by exsanguination under sevoflurane 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
Changes in estrous cyclicity, copulation index and fertility index were analyzed by Fisher's test. G raded pathological data was analyzed by Mann-Whitney's U test (significance level = 0.05) and pathol ogical data with number of positive and negative animals was analyzed by one-sided Fisher's test. Ot her data obtained values in each animal or mean of a litter was one data, and these data were compar ed among the satellite groups and other among the groups. These data were analyzed using F-test for homogeneity of distribution. The Student's t-test and the Aspin-Welch's t-test were conducted for homogenous and non-homogenous distribution, respectively to compare the control and individu al treatment groups. Three or more groups setting, these data were analyzed using Bartlett's test for homogeneity of distribution. The Dunnett's multiple comparison test after the ANOVA and the Dunnett's-type mean rank sum test after Kruskal-Wallis's H test were conducted for homogenous an d non-homogenous distribution, respectively to compare the control and individual treatment groups. Significance level was set at 0.05 compared with the control group and among the groups.

Reproductive indices
Each parameter was determined by the following equations:
Copulation index (%) = (No. of copulated pares / No. of mated pares) × 100
Fertility index (%) = (No. of fertile males / No. of copulated pares) × 100
Delivery index (dams, %) = (No. of dams with live offspring / No. of pregnant dams) × 100
Implantation index (%) = (No. of implantation scars / No. of corpora lutea) × 100
Sex ratio = No. of male offspring / (No. of male offspring + No. of female offspring)
Delivery index (offspring) = (No. of offspring at birth/ No. of implantation scars) × 100
Birth index = (No. of live offspring at birth/No. of implantation scars) × 100
Live birth index = (No. of live offspring at birth/No. of offspring at birth) × 100

Offspring viability indices
Viability index = (No. of live offspring 4days after birth / No. of live offspring at birth) × 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)
not examined

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
effects observed, treatment-related

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

Urinalysis findings
effects observed, treatment-related

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

Behaviour (functional findings)
no effects observed

Immunological findings
not examined

Organ weight findings including organ / body weight ratios
no effects observed

Gross pathological findings
no effects observed

Neuropathological findings
not examined

Histopathological findings: non-neoplastic
no effects observed

Histopathological findings: neoplastic
not examined

Reproductive function / performance (P0)

Reproductive function: oestrous cycle
no effects observed

Reproductive function: sperm measures
no effects observed

Reproductive performance
no effects observed

Details on results (P0)

General toxicity: See 7.5.1 Repeated dose toxicity.001
Reproductive function / performance: no effects observed

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/female

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

Key result
false

Dose descriptor
NOAEL

Effect level

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

Based on
test mat.

Sex
male

Basis for effect level
haematology
A significant prolongation of PT and a trend toward prolongation of APTT were observed in males at 250 mg/kg bw/day and above.
clinical biochemistry
A significant increase in LDH was observed in males at 250 mg/kg bw/day and above.

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
urinalysis
Significant decreases in urine volume, sodium, potassium, and chloride excretion were observed in non-mated females at 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
no effects observed

Gross pathological findings
no effects observed

Details on results (F1)

No effects observed.

Effect levels (F1)

Key result
false

Dose descriptor
NOAEL

Generation
F1

Effect level

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

Based on
test mat.

Sex
male/female

Basis for effect level
other:
There were no effects on developmental parameters up to 1000 mg/kg bw/day.

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/PDF58670-89-6d.pdf

Applicant's summary and conclusion

Conclusions
A combined repeated oral dose toxicity study with the reproduction/developmental toxicity screening test was performed according to a Japanese guideline (similar to OECD TG 422). There were no effects on the reproductive and developmental parameters up to 1000 mg/kg bw/day. The NOAEL for the rat reproductive/developmental toxicity of 2-decyltetradecanol was regarded as 1000 mg/kg bw/day, the highest dose tested.

References

Reference Substances

REFERENCE_SUBSTANCE: 2-decyltetradecanol

UUID: ECB5-ed0a3e06-c7c8-45c8-809e-469a2979924d
Dossier UUID:
Author:
Date: 2023-01-13T10:44:00.000+09:00
Remarks:

Reference substance name
2-decyltetradecanol

IUPAC name
2-decyltetradecan-1-ol

Inventory

Inventory number

Inventory name
2-decyltetradecanol

Inventory
EC Inventory

Inventory number
261-385-0

CAS number
58670-89-6

Molecular formula
C24H50O

Description

CAS number
58670-89-6

Synonyms

Synonyms

Identity
1-Tetradecanol, 2-decyl-

Identity
1-Tetradecanol, 2-decyl-

Molecular and structural information

Molecular formula
C24H50O

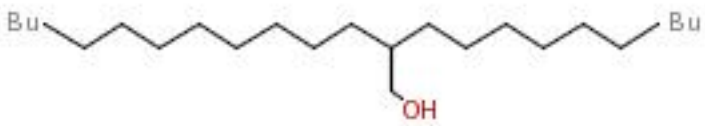
Molecular weight

354.6532

SMILES notation
CCCCCCCCCCCCC(CO)CCCCCCCCCC

InChI
InChI=1/C24H50O/c1-3-5-7-9-11-13-14-16-18-20-22-24(23-25)21-19-17-15-12-10-8-6-4-2/h24-25H
,3-23H2,1-2H3

Structural formula



Test Materials

TEST_MATERIAL_INFORMATION: 2-Decyltetradecanol

UUID: a0e6e333-0eed-44e4-99a8-a45917a54c4c
Dossier UUID:
Author:
Date: 2023-01-13T10:44:08.000+09:00
Remarks:

Name
2-Decyltetradecanol

Composition

Composition

Type
Constituent

Reference substance
2-decyltetradecanol / 2-decyltetradecan-1-ol / 58670-89-6 / 261-385-0

EC number	EC name
261-385-0	EC Inventory
CAS number	**CAS name**
58670-89-6	
IUPAC name	
2-decyltetradecan-1-ol	

Concentration

98.4	% (v/v)

Literatures

LITERATURE: Combined repeat dose and reproductive/ developmental toxicity screening test of 2-decyltetradecanol oral administration in rats

UUID: 138047cc-9b02-48b4-8507-46a113fe884e
Dossier UUID:
Author:
Date: 2022-12-01T15:38:23.000+09:00
Remarks:

General information

Reference Type
study report

Title
Combined repeat dose and reproductive/developmental toxicity screening test of 2-decyltetradecanol oral administration in rats

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

Year
2013

Bibliographic source
available in the web of Japan Existing Chemical Data Base (JECDB) at https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF58670-89-6d.pdf

Testing facility
the Hatano Research Institute, Food and Drug Safety Center

Report date
2013-09-25

Report number
R-12-016

LITERATURE: In Vitro Chromosomal Aberration Test of 2-Decyltetradecanol on Cultured Chinese Hamster Cells.

UUID: 36c464ef-e046-40b1-818f-09c352ee65eb
Dossier UUID:
Author:
Date: 2023-01-10T16:35:08.000+09:00
Remarks:

General information

Reference Type
study report

Title
In Vitro Chromosomal Aberration Test of 2-Decyltetradecanol on Cultured Chinese Hamster Cells.

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

Year
2013

Bibliographic source
Japan Existing Chemical Data Base (JECDB) https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF58670-89-6f.pdf

Testing facility
the Hatano Research Institute, Food and Drug Safety Center

Report date
2013-04-09

Report number
G-12-012

LITERATURE: Reverse Mutation Test of 2-Decyltetradecanol on Bacteria.

UUID: 0704af16-c457-4971-9eb5-eb3d28379e39
Dossier UUID:
Author:
Date: 2023-01-10T15:56:46.000+09:00
Remarks:

General information

Reference Type
study report

Title
Reverse Mutation Test of 2-Decyltetradecanol on Bacteria.

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

Year
2013

Bibliographic source
Japan Existing Chemical Data Base (JECDB) https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF1459-93-4e.pdf

Testing facility
the Hatano Research Institute, Food and Drug Safety Center

Report date
2013-03-22

Report number
M-12-023