



Name: 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide / 35948-25-5

Legal entity owner: National Institute of Health Sciences, Japan

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6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide

CORE

General information

FIXED_RECORD: Assessment approach

UUID: 14943975-28d0-3382-9568-68bab6137bc3

Dossier UUID:

Author: SuperUser

Date: 2020-03-24T16:05:30.000+09:00

Remarks:

OECD

Health Effects

Repeated dose toxicity: oral

ENDPOINT_STUDY_RECORD: Repeated dose toxicity: oral.001

UUID: ad630bf8-f3b8-4e14-8f21-5e6133267b5c

Dossier UUID:

Author: SuperUser

Date: 2020-10-01T12:09:31.851+09:00

Remarks:

Administrative data

Endpoint

short-term repeated dose toxicity: oral

Type of information

experimental study

Adequacy of study

key study

Robust study summary

false

Used for classification

false

Used for SDS

false

Reliability

1 (reliable without restriction)

Rationale for reliability incl. deficiencies

other: The study was conducted in accordance with Test Guidelines and under GLP

Cross-reference

Reason / purpose

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

Related information

[OECD / Toxicity to reproduction / Toxicity to reproduction.001 / 6H-dibenz\[c,e\]\[1,2\]oxaphosphorin 6-oxide / 35948-25-5](#)

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

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

[6H-dibenz\[c,e\]\[1,2\]oxaphosphorin 6-oxide](#)

Specific details on test material used for the study

- Name of test material (as cited in study report): 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide
- Analytical purity: 99.4%
- Storage condition of test material: Cold and dark place (3 - 6°C)
- Stability under test conditions: The stability of test material was identified by analysis of the remainder.

Test animals

Species

rat

common rodent species

Strain

other: Crl:CD(SD)

Sex

male/female

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

- Source: Charles River Japan, Inc., Atsugi Breeding Center.
- Age at study initiation: 10 weeks old
- Weight at study initiation: Male: 384 g (359-409 g), Female: 236 g (212-265 g)
- Housing: Animals were individually housed in bracket-type metallic wire-mesh cages (254W × 350D × 170H mm), from gestation day 17 to lactation day 4, Dams were bred individually or with individual littermates in plastic cages (340W x 400D x 185H mm) and bedding.
- Diet: Solid feed (NMF: Oriental Yeast Co., Ltd.) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation period: 17 days

ENVIRONMENTAL CONDITIONS

- Temperature (°C): 23±3 (actual temperature: 22-26°C)

- Humidity (%): 50±20% (actual humidity: 38-61%)
- Air changes (per hr): 10-15
- 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): 5 mL/kg
- Dosing volume: 5 mL/kg

Analytical verification of doses or concentrations

yes

Details on analytical verification of doses or concentrations

Test suspensions at each concentration to be used for males in week 1 and six week of administration were analyzed by absorption spectrophotometry method at BoZo Research Center Inc. Results showed that the concentration of test article in each concentration was 102.0 to 105.7% of the nominal concentration and both values were within the acceptable range (concentration: percentage of nominal concentration, 100±10%)

Duration of treatment / exposure

(P) Males: 42 days including 14 days pre-mating

(P) Females: 41-46 days including 14 days pre-mating, mating and gestation periods and the days until day 4 of lactation

Female (no 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.	
100	mg/kg bw/day (actual dose received)
Dose / conc.	
300	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 group: 12 females/dose (0, 100, 300, and 1000 mg/kg bw/day), 7, 12, 12, and 7 males/dose (0, 100, 300, and 1000 mg/kg bw/day)

Satellite group: 5 females/dose (0 and 1000 mg/kg bw/day)

Recovery group: 5 males/dose and 5 females (satellite group)/dose (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 highest dose of 1000 mg/kg bw/day was selected as an expected obvious toxic dose, and the lowest dose of 100 mg/kg bw/day was selected as an expected no toxic dose. The middle dose levels of 300 mg/kg bw/day were selected.

[14-day preliminary study]

A 14-day repeated dose oral toxicity test (CrI:CD(SD) rats, doses: 0, 100, 300 or 1000 mg/kg bw/day). In the 300 mg/kg bw/day or more, decrease in total protein was observed. In the 1000 mg/kg bw/day, decrease in red blood cell count, hemoglobin and hematocrit value were observed.

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

Examinations

Observations and examinations performed and frequency

CAGE SIDE OBSERVATIONS: Yes

- Time schedule: 3 times/day (before administration, immediately after administration and 2 hours after administration) during the administration period. Once a day during the recovery period.

DETAILED CLINICAL OBSERVATIONS: Yes

- Time schedule:

Male main and female satellite groups: once before the start of administration, once every weekly during the administration.

Female main group: once before the start of administration, days 1, 7, 14 and 20 of gestation, and day 4 of lactation.

Male and female recovery groups: once before the start of administration, once every weekly during the administration and recovery periods.

BODY WEIGHT: Yes

- Time schedule for examinations:

Males in the main and females satellite groups were weighed on days 1, 4, 8, 11, 15, 18, 22, 25, 29, 32, 36, 39 and 42 of administration and on the day of necropsy, and males and females in the recovery groups were weighed on days 1, 4, 8, 11 and 14 of recovery and on the day of necropsy in addition to the measurement days for males in the main groups.

Females in the main groups were weighed on days 1, 4, 8, 11 and 15 of administration (uncopulated animals were weighed on days 18 and 22 of administration as well), days 0, 4, 7, 11, 14, 17 and 20 of gestation, days 0 and 4 of lactation and the day of necropsy.

FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):

- Food consumption: Yes

Measurement of food consumption was conducted on all animals at the following frequencies: males in the main and females satellite groups on days 1, 4, 8, 11, 15, 32, 36, 39 and 42 of administration; males and females in the recovery groups on days 1, 4, 8, 11 and 14 of recovery in addition to the measurement days for males in the main groups; and females in the main groups on days 1, 4, 8, 11 and 15 of administration, days 1, 4, 7, 11, 14, 17 and 20 of gestation and days 2 and 4 of lactation.

OPHTHALMOSCOPIC EXAMINATION: No

HAEMATOLOGY: Yes

- Time schedule for collection of blood: At the end of administration period, or at the end of recovery period in both sexes

- Anaesthetic used for blood collection: ether

- Animals fasted: Yes

- How many animals:

All animals/sex/group (Control and 1000 mg/kg/day),

5 animals/sex/group (100 and 300 mg/kg/day)

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

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:

All animals/sex/group (Control and 1000 mg/kg/day),

5 animals/sex/group (100 and 300 mg/kg/day)

- Parameters checked: ALP, total cholesterol, triglyceride, phospholipids, total bilirubin, glucose, blood urea nitrogen, creatinine, sodium, potassium, chloride, calcium, inorganic phosphorus, total protein, albumin, A/G ratio, AST (GOT), ALT (GPT), LDH, γ -GTP

URINALYSIS: Yes

- Time schedule for collection of urine: final week of administration (days 36 to 37 of administration) and in the final week of recovery (days 8 to 9 of recovery)

- Metabolism cages used for collection of urine: Yes

A urine collector to collect four-hour urine samples under fasting but ad libitum drinking conditions, followed by collection of 20-hour urine samples under ad libitum feeding and drinking conditions.

- How many animals: 5 animals/group

- Parameters checked: pH, protein, ketones, glucose, occult blood, bilirubin, urobilinogen, color, sediment, urine volume (4-hour volume), osmotic pressure, urine volume (20-hour volume), water intake (24-hour volume)

BLOOD HORMONE: Yes

- Time schedule for collection of serum: Same as clinical chemistry

- Animals fasted: Yes

- How many animals:

All animals/sex/group (Control and 1000 mg/kg/day),

5 animals/sex/group (100 and 300 mg/kg/day)

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

NEUROBEHAVIOURAL EXAMINATION: Yes

- Time schedule for examinations:

Males in the main groups: final week of administration (day 40 of administration)

Females in the main groups: lactation day 4 (day 42 to day 44 of administration) after necropsy of F1 pups

Males and females in the recovery groups: final week of administration (day 40 of administration) and in the final week of recovery (day 12 of recovery).

- Dose groups that were examined: All dose groups (5 animals/sex/group)

- Battery of functions tested:

1) Manipulative Test. Auditory response, approach response, touch response, tail pinch response, pupillary reflex, aerial righting reflex, landing foot splay

2) Measurement of Grip Strength. Following manipulative test, grip strength of forelimb and hind limb was measured by CPU gauge MODEL-RX-5 (AIKOH Engineering Co., Ltd.).

3) Measurement of Motor Activity. Following measurement of grip strength, motor activity was measured by a motor activity sensor for experimental animals NS-AS01 (Neuro Science, Inc). The measurement was conducted for 1 hour, and measured values at 10-minute intervals and from 0 to 60 minutes were collected.

Sacrifice and pathology

GROSS PATHOLOGY: Yes

ORGAN WEIBHT: Yes [brain, pituitary, thyroids (including parathyroids), adrenal gland, thymus, spleen, heart, liver, kidney, testis, epididymis, ovary, uterus]

HISTOPATHOLOGY: Yes, [cerebrum, cerebellum (including pons) , pituitary, spinal cord (thoracic), sciatic nerve, eye ball, thyroid, parathyroid, adrenal glands, thymus, spleen, submandibular lymph nodes, mesenteric lymph nodes, heart, trachea, lung (including bronchial), stomach, duodenum, jejunum, ileum, cecum, colon, rectum, liver, kidney, bladder, testis, epididymis, ovary, uterus, vagina, prostate, seminal vesicles, sternum and femur (including bone marrows),and macroscopic lesions]

Statistics

The data were analyzed for homogeneity of variance by the Bartlett test. If variances were homogeneous, data was analyzed by the Dunnett test, whereas heterogeneous data was analyzed by the Dunnett type mean rank test ($p < 0.05$, two-sided).

In the recovery test, these values of two groups were analyzed by F test. If variances were homogeneous, data was analyzed by the Student t-test, whereas heterogeneous data was analyzed by the Aspin-Welch t-test ($p < 0.05$, two-sided).

Results and discussion

Results of examinations

Clinical signs

no effects observed

Mortality

no mortality observed

Body weight and weight changes

effects observed, treatment-related

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

no effects observed

Clinical biochemistry findings

no effects observed

Description (incidence and severity)

Including blood hormones (T3, T4, TSH)

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

effects observed, treatment-related

Neuropathological findings

not examined

Histopathological findings: non-neoplastic

effects observed, treatment-related

Histopathological findings: neoplastic

not examined

Details on results**CLINICAL SIGNS AND MORTALITY:**

Mortality: There was no death.

Clinical signs: There were no effects 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 periods.

BODY WEIGHT:

A decrease in body weight gain was observed from the second week of administration in males receiving 1000 mg/kg bw/day.

Slight decrease in body weight gain was observed during pregnancy in mating females receiving 1000 mg/kg bw/day.

FOOD CONSUMPTION:

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

URINALYSIS:

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

NEUROBEHAVIOURAL EXAMINATION: There were no changes related to the test substance in any groups at the dosing and recovery periods.

HAEMATOLOGY:

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

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.

ORGAN WEIGHTS:

[At the end of dosing period]:

Decreases in absolute and relative weights of thymus were observed in non-mating females receiving 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:

[At the end of dosing period]:

Forestomach: Focus raised region and focus dark red region were observed in mating females receiving 100 mg/kg bw/day and above, and in males receiving 300 mg/kg bw/day and above. Thickening of limiting ridge was observed in mating and non-mating females receiving 1000 mg/kg bw/day.

[At the end of recovery period]: There were no changes related to the test substance in any groups.

HISTOPATHOLOGY: NON-NEOPLASTIC:

[At the end of dosing period]:

Forestomach: Erosion/ulcer and edema of mucosal/submucosal were observed in mating females receiving 100 mg/kg bw/day and above and in males receiving 300 mg/kg bw/day and above. Hyperplasia of squamous cells were observed in males and mating females receiving 100 mg/kg bw/day and above. Degeneration/necrosis of squamous cells were observed in males receiving 100 mg/kg bw/day and above and in mating females receiving 300 mg/kg bw/day and above. These findings were also observed in non-mating females receiving 1000 mg/kg bw/day.

Cecum: Single cell necrosis and diffuse hyperplasia of mucosa were observed in males and mating females receiving 300 mg/kg bw/day. These findings were also observed in non-mating females receiving 1000 mg/kg bw/day.

[At the end of recovery period]:

Cecum: Single cell necrosis and diffuse hyperplasia of mucosa were persisted in males receiving 1000 mg/kg bw/day, but to a lesser degree.

Effect levels

Key result true		
Dose descriptor LOAEL		
Effect level	100	mg/kg bw/day (actual dose received)
Based on test mat.		
Sex male/female		
Basis for effect level histopathology: non-neoplastic Forestomach lesions were observed in males and females receiving 100 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/PDF35948-25-5d.pdf

Applicant's summary and conclusion

Conclusions

Based on the effects of 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide on the stomach, the LOAEL for repeated oral dosing was determined to be 100 mg/kg bw/day.

Executive summary

A combined repeated-dose toxicity study with the reproduction/developmental toxicity screening test was done according to OECD TG 422. Male and female rats (12 animals/sex/dose) were administered with 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide via oral gavage at doses of 0 [vehicle: corn oil], 100, 300, and 1,000 mg/kg bw/day. Males (12/dose) were then treated with 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide for 42 days, which include a 14-day pre-mating period and a subsequent mating period, while females (12/dose) were treated for 41–46 days, which include a 14-day pre-mating, mating and gestation periods until lactation day 4. Among the 12 males administered with 0 and 1,000 mg/kg bw/day, 5 were assigned as recovery group. Additional 10 females treated with 0 and 1,000 mg/kg bw/day were assigned as a satellite group and treated with 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide for 42 days, with no mating, and examined after a 14-day recovery period.

No deaths were recorded, and no changes in clinical signs, manipulative test, grip strength, motor activity, body weight, food consumption, urinalysis, hematology, blood chemistry as a result of treatment in any of the dose groups for both males and females at the end of the treatment and recovery periods. There was a decrease in body weight gain in males receiving 1,000 mg/kg bw/day after 2 weeks of administration, and a statistically significant decreased body weight gain was observed in the mating group females receiving 1,000 mg/kg bw/day in the gestation period. The absolute and relative weights of the thymus were significantly decreased in the satellite group females receiving 1,000 mg/kg bw/day at the end of the administration period. In the gross pathological examination of males receiving ≥ 300 mg/kg bw/day, a raised and dark red forestomach was seen. Additionally, there was thickening of the limiting ridge of the forestomach in females receiving 100 mg/kg bw/day at the end of the administration period. Histopathological findings show an erosion/ulcer and edema in the mucosa/submucosa of the forestomach in females receiving 100 mg/kg bw/day and both males and females receiving ≥ 300 mg/kg bw/day, and degeneration/necrosis of squamous cells of the forestomach was indicated in males receiving 100 mg/kg bw/day and both males and females receiving ≥ 300 mg/kg bw/day. There was also a hyperplasia of squamous cells of the forestomach in both males and females at ≥ 100 mg/kg bw/day. These histopathological findings in the forestomach mean that there is a mucosal irritation by the test substance. Single-cell necrosis and diffuse hyperplasia of cecum mucosa were seen in both males and females at ≥ 300 mg/kg bw/day. Since the changes observed in the organ weight and histopathological examination were lessened or disappeared at the end of the recovery period, they are thought to be reversible. With these effects of the forestomach at 100 mg/kg bw/day in males and females, the NOEL for repeated-dose toxicity of 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide was 100 mg/kg bw/day in rats.

Genetic toxicity in vitro

ENDPOINT_STUDY_RECORD: Genetic toxicity in vitro.001

UUID: 65ccc5a2-98eb-46de-816c-5418bf6fb04b

Dossier UUID:

Author: SuperUser

Date: 2020-03-26T15:47:12.246+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 6H-dibenz\[c,e\]\[1,2\]oxaphosphorin 6-oxide 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

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

Deviations

no

GLP compliance

yes

Type of assay

bacterial reverse mutation assay
in vitro gene mutation study in bacteria

Test material**Test material information**

[6H-dibenz\[c,e\]\[1,2\]oxaphosphorin 6-oxide](#)

Specific details on test material used for the study

Purity 99.4%

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

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

Species / strain / cell type

E. coli WP2 uvr A pKM 101
bacteria

Metabolic activation

with and without

Metabolic activation system

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

Test concentrations with justification for top dose

-S9 mix:

156, 313, 625, 1250, 2500, 5000 µg/plate (TA100, TA1535, TA98 strains)

39.1, 78.1, 156, 313, 625, 1250 µg/plate (TA1537 strain)

156, 313, 625, 1250, 2500, 5000 µg/plate (WP2uvrA/pKM101 strain)

+S9 mix:

313, 625, 1250, 2500, 5000 µg/plate (TA100, TA98 strains)

156, 313, 625, 1250, 2500, 5000 µg/plate (TA1535, TA1537 strains)

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

Maximum concentration was established based on the result of the preliminary test at concentration up to 5000 µg/plate. In this test, the growth inhibition was observed at 1250 µg/plate and above for S. typhimurium TA1537 without S9 mix, at 5000 µg/plate for S. typhimurium TA100, TA1535, TA 98, and E. coli WP2 uvrA without S9 mix, and S. typhimurium TA 1535 and TA1537 with S9 mix.

Vehicle / solvent

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

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, sodium azide and 2-Methoxy-6-chloro-9-[3-(2-chloroethyl)-aminopropylamino]acridine 2HCl; +S9 mix: 2-aminoanthracene, benzo(a)pyrene

Details on test system and experimental conditions

METHOD OF APPLICATION: Preincubation

DURATION- Preincubation period: 20 min at 37°C

- Exposure duration: 48 or 49 hrs

NUMBER OF PLATES: 3

NUMBER OF REPLICATIONS: 2

DETERMINATION OF CYTOTOXICITY

- Method: other: growth inhibition

Evaluation criteria

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

Statistics

no

Results and discussion

Test results**Key result**

true

Species / strain

S. typhimurium TA 1535
bacteria

Metabolic activation

with and without

Genotoxicity

negative

Cytotoxicity / choice of top concentrations

cytotoxicity -S9 mix: 5000 µg/plate; +S9 mix: 5000 µg/plate

Vehicle controls validity

valid

Untreated negative controls validity

not examined

Positive controls validity

valid

Key result

true

Species / strain

S. typhimurium TA 1537
bacteria

Metabolic activation

with and without

Genotoxicity

negative

Cytotoxicity / choice of top concentrations

cytotoxicity -S9 mix: 1250 µg/plate; +S9 mix: 2500 µg/plate or more

Vehicle controls validity

valid

Untreated negative controls validity

not examined

Positive controls validity

valid

Key result

true

Species / strain

S. typhimurium TA 98
bacteria

Metabolic activation

with and without

Genotoxicity

negative

Cytotoxicity / choice of top concentrations

cytotoxicity -S9 mix: 5000 µg/plate

Vehicle controls validity

valid

Untreated negative controls validity

not examined

Positive controls validity

valid

Key result

true

Species / strain

S. typhimurium TA 100
bacteria

Metabolic activation

with and without

Genotoxicity

negative

Cytotoxicity / choice of top concentrations

cytotoxicity -S9 mix: 2500 µg/plate or more (test 2: 5000 µg/plate)

Vehicle controls validity

valid

Untreated negative controls validity

not examined

Positive controls validity

valid

Key result

true

Species / strain

E. coli WP2 uvr A pKM 101
bacteria

Metabolic activation

with and without

Genotoxicity

negative

Cytotoxicity / choice of top concentrations

cytotoxicity -S9 mix: 5000 µg/plate

Vehicle controls validity

valid

Untreated 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/PDF35948-25-5e.pdf

Please also see the attached files (Tables in English)

Overall remarks, attachments

Attached background material**Attached document**

35948255.xlsx / 35.33 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 TA1537, and *Escherichia coli* WP2uvrA/pKM101 (OECD TG 471), 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide was negative with or without metabolic activation.

ENDPOINT_STUDY_RECORD: Genetic toxicity in vitro.002

UUID: 4a40f69a-43f6-4948-8da2-6d606b8c0219

Dossier UUID:

Author: SuperUser

Date: 2019-12-19T11:53:31.000+09:00

Remarks:

Administrative data

Endpoint

in vitro cytogenicity / chromosome aberration study in mammalian cells

Type of information

experimental study

Adequacy of study

key study

Robust study summary

false

Used for classification

false

Used for SDS

false

Reliability

1 (reliable without restriction)

Rationale for reliability incl. deficiencies

other: OECD Test Guideline study under GLP condition

Data source

Reference

[In Vitro Chromosomal Aberration Test of 6H-dibenz\[c,e\]\[1,2\]oxaphosphorin 6-oxide on Cultured Chinese... / Ministry of Health, Labour and Welfare \(MHLW\), Japan / study report](#)

Data access

data published

Materials and methods

Test guideline

Qualifier

according to

Guideline

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

Deviations

no

Qualifier

according to

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**

[6H-dibenz\[c,e\]\[1,2\]oxaphosphorin 6-oxide](#)

Specific details on test material used for the study

Purity 99.4%

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

Test concentrations with justification for top dose

Cell growth inhibition study

-S9 mix (short-term treatment): 17.2, 34.4, 68.8, 138, 275, 550, 1100, 2200 ug/mL (IC50=1457.5 ug/mL)

+S9 mix (short-term treatment): 17.2, 34.4, 68.8, 138, 275, 550, 1100, 2200 ug/mL (IC50=1200.0 ug/mL)

-S9 mix (continuous treatment, 24hr): 17.2, 34.4, 68.8, 138, 275, 550, 1100, 2200 ug/mL (IC50=902.0 ug/mL)

-S9 mix (continuous treatment, 48hr): 17.2, 34.4, 68.8, 138, 275, 550, 1100, 2200 ug/mL (IC50=811.9 ug/mL)

Main study

-S9 (short-term treatment): 275, 550, 1100, 2200 ug/mL

+S9 (short-term treatment): 275, 550, 1100, 2200 ug/mL

-S9 (continuous treatment, 24hr): 275, 550, 1100, 2200 ug/mL

-S9 (continuous treatment, 48hr): 275, 550, 1100, 2200 ug/mL

Vehicle / solvent

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

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]: cyclophosphamide

Details on test system and experimental conditions

METHOD OF APPLICATION: Exposure duration: [short-term treatment]: 6 hrs + 18 hr, [continuous treatment]: 24, 48 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(\pm): 5% or more and less than 10%, Positive(+): 10% or more

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

Untreated 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/PDF35948-25-5f.pdf

Applicant's summary and conclusion _____

Conclusions

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

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

Toxicity to reproduction

ENDPOINT_STUDY_RECORD: Toxicity to reproduction.001

UUID: f41cabd7-dc43-4c7d-baff-ade412356203

Dossier UUID:

Author: SuperUser

Date: 2020-10-01T12:14:04.934+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

other: OECD Test Guideline study under GLP condition

Cross-reference

Reason / purpose

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

Related information

[OECD / Repeated dose toxicity: oral / Repeated dose toxicity: oral.001 / 6H-dibenz\[c,e\]\[1,2\]oxaphosphorin 6-oxide / 35948-25-5](#)

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

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

[6H-dibenz\[c,e\]\[1,2\]oxaphosphorin 6-oxide](#)

Specific details on test material used for the study

- Name of test material (as cited in study report): 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide
- Analytical purity: 99.4%
- Storage condition of test material: Cold and dark place (3 - 6°C)
- Stability under test conditions: The stability of test material was identified by analysis of the remainder.

Test animals

Species

rat

Strain

other: Crl:CD(SD)

Sex

male/female

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

- Source: Charles River Japan, Inc., Atsugi Breeding Center.
- Age at study initiation: 10 weeks old
- Weight at study initiation: Male: 384 g (359-409 g), Female: 236 g (212-265 g)
- Housing: Animals were individually housed in bracket-type metallic wire-mesh cages (254W × 350D × 170H mm), from gestation day 17 to lactation day 4, Dams were bred individually or with individual littermates in plastic cages (340W x 400D x 185H mm) and bedding.
- Diet: Solid feed (NMF: Oriental Yeast Co., Ltd.) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation period: 19 days

ENVIRONMENTAL CONDITIONS

- Temperature (°C): 23±3 (actual temperature: 22-26°C)
- Humidity (%): 50±20% (actual humidity: 38-61%)
- Air changes (per hr): 10-15
- 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): 5 mL/kg
- Dosing volume: 5 mL/kg

Details on mating procedure

- M/F ratio per cage: 1/1
- Length of cohabitation: up to 5 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

Test suspensions at each concentration to be used for males in week 1 and six week of administration were analyzed by absorption spectrophotometry method at BoZo Research Center Inc. Results showed that the concentration of test article in each concentration was 102.0 to 105.7% of the nominal concentration and both values were within the acceptable range (concentration: percentage of nominal concentration, 100±10%)

Duration of treatment / exposure

(P) Males: 42 days including 14 days pre-mating

(P) Females: 41-46 days including 14 days pre-mating, mating and gestation periods and the days until day 4 of lactation

Female (no 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.	
100	mg/kg bw/day (actual dose received)
Dose / conc.	
300	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 group: 12 females/dose (0, 100, 300, and 1000 mg/kg bw/day), 7, 12, 12, and 7 males/dose (0, 100, 300, and 1000 mg/kg bw/day)

Satellite group: 5 females/dose (0 and 1000 mg/kg bw/day)

Recovery group: 5 males/dose and 5 females (satellite group)/dose (0 and 1000 mg/kg bw/day)

Control animals

yes, concurrent no treatment

Details on study design

- Dose selection rationale: Based on the results of a 14-day preliminary study, the highest dose of 1000 mg/kg bw/day was selected as an expected obvious toxic dose, and the lowest dose of 100 mg/kg bw/day was selected as an expected no toxic dose. The middle dose levels of 300 mg/kg bw/day were selected.

[14-day preliminary study]

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

In the 300 mg/kg bw/day or more, decrease in total protein was observed. In the 1000 mg/kg bw/day, decrease in red blood cell count, hemoglobin and hematocrit value were observed.

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

Examinations**Parental animals: Observations and examinations**

CAGE SIDE OBSERVATIONS: Yes

- Time schedule: 3 times/day (before administration, immediately after administration and 2 hours after administration) during the administration period. Once a day during the recovery period.

DETAILED CLINICAL OBSERVATIONS: Yes

- Time schedule:

Male main and female satellite groups: once before the start of administration, once every weekly during the administration.

Female main group: once before the start of administration, days 1, 7, 14 and 20 of gestation, and day 4 of lactation.

Male and female recovery groups: once before the start of administration, once every weekly during the administration and recovery periods.

BODY WEIGHT: Yes

- Time schedule for examinations:

Males in the main and females satellite groups were weighed on days 1, 4, 8, 11, 15, 18, 22, 25, 29, 32, 36, 39 and 42 of administration and on the day of necropsy, and males and females in the recovery groups were weighed on days 1, 4, 8, 11 and 14 of recovery and on the day of necropsy in addition to the measurement days for males in the main groups.

Females in the main groups were weighed on days 1, 4, 8, 11 and 15 of administration (uncopulated animals were weighed on days 18 and 22 of administration as well), days 0, 4, 7, 11, 14, 17 and 20 of gestation, days 0 and 4 of lactation and the day of necropsy.

FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):

- Food consumption: Yes

Measurement of food consumption was conducted on all animals at the following frequencies:

males in the main and females satellite groups on days 1, 4, 8, 11, 15, 32, 36, 39 and 42 of administration; males and females in the recovery groups on days 1, 4, 8, 11 and 14 of recovery in addition to the measurement days for males in the main groups; and females in the main groups on days 1, 4, 8, 11 and 15 of administration, days 1, 4, 7, 11, 14, 17 and 20 of gestation and days 2 and 4 of lactation.

OPHTHALMOSCOPIC EXAMINATION: No

HAEMATOLOGY: Yes

- Time schedule for collection of blood: At the end of administration period, or at the end of recovery period in both sexes
- Anaesthetic used for blood collection: ether
- Animals fasted: Yes
- How many animals:
All animals/sex/group (Control and 1000 mg/kg/day),
5 animals/sex/group (100 and 300 mg/kg/day)
- Parameters examined: red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, reticulocyte percentage, platelet count, white blood cell count, differential white blood cell count, absolute number of each white blood cell, prothrombin time, activated partial thromboplastin time, fibrinogen.

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:
All animals/sex/group (Control and 1000 mg/kg/day),
5 animals/sex/group (100 and 300 mg/kg/day)
- Parameters checked: ALP, total cholesterol, triglyceride, phospholipids, total bilirubin, glucose, blood urea nitrogen, creatinine, sodium, potassium, chloride, calcium, inorganic phosphorus, total protein, albumin, A/G ratio, AST (GOT), ALT (GPT), LDH, γ -GTP

URINALYSIS: Yes

- Time schedule for collection of urine: final week of administration (days 36 to 37 of administration) and in the final week of recovery (days 8 to 9 of recovery)
- Metabolism cages used for collection of urine: Yes
A urine collector to collect four-hour urine samples under fasting but ad libitum drinking conditions, followed by collection of 20-hour urine samples under ad libitum feeding and drinking conditions.
- How many animals: 5 animals/group
- Parameters checked: pH, protein, ketones, glucose, occult blood, bilirubin, urobilinogen, color, sediment, urine volume (4-hour volume), osmotic pressure, urine volume (20-hour volume), water intake (24-hour volume)

BLOOD HORMONE: Yes

- Time schedule for collection of serum: Same as clinical chemistry
- Animals fasted: Yes
- How many animals:
All animals/sex/group (Control and 1000 mg/kg/day),
5 animals/sex/group (100 and 300 mg/kg/day)
- Parameters checked: Triiodothyronine (T3), Thyroxin (T4), and thyroid stimulating hormone (TSH)

NEUROBEHAVIOURAL EXAMINATION: Yes

- Time schedule for examinations:
Males in the main groups: final week of administration (day 40 of administration)
Females in the main groups: lactation day 4 (day 42 to day 44 of administration) after necropsy of F1 pups
Males and females in the recovery groups: final week of administration (day 40 of administration) and in the final week of recovery (day 12 of recovery).
- Dose groups that were examined: All dose groups (5 animals/sex/group)
- Battery of functions tested:
 - 1) Manipulative Test. Auditory response, approach response, touch response, tail pinch response, pupillary reflex, aerial righting reflex, landing foot splay
 - 2) Measurement of Grip Strength. Following manipulative test, grip strength of forelimb and hind limb was measured by CPU gauge MODEL-RX-5 (AIKOH Engineering Co., Ltd.).

3) Measurement of Motor Activity. Following measurement of grip strength, motor activity was measured by a motor activity sensor for experimental animals NS-AS01 (Neuro Science, Inc). The measurement was conducted for 1 hour, and measured values at 10-minute intervals and from 0 to 60 minutes were collected.

Oestrous cyclicity (parental animals)

Vaginal smears were collected from all females in the main 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, 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 ether anesthesia. SACRIFICE: Male main and female satellite animals: On next day after the last administration (Day 43), Maternal animals: on Day 4 of lactation, and male and females recovery animals: on Day 14 of recovery.

GROSS PATHOLOGY: Yes

ORGAN WEIGHT: Yes [brain, pituitary, thyroids (including parathyroids), adrenal gland, thymus, spleen, heart, liver, kidney, testis, epididymis, ovary, uterus]

HISTOPATHOLOGY: Yes, [cerebrum, cerebellum (including pons), pituitary, spinal cord (thoracic), sciatic nerve, eye ball, thyroid, parathyroid, adrenal glands, thymus, spleen, submandibular lymph nodes, mesenteric lymph nodes, heart, trachea, lung (including bronchial), stomach, duodenum, jejunum, ileum, cecum, colon, rectum, liver, kidney, bladder, testis, epididymis, ovary, uterus, vagina, prostate, seminal vesicles, sternum and femur (including bone marrows), and macroscopic lesions]

Postmortem examinations (offspring)

SACRIFICE

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

GROSS NECROPSY: Yes

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

HISTOPATHOLOGY / ORGAN WEIGHTS

- Not examined.

Statistics

The data were analyzed for homogeneity of variance by the Bartlett test. If variances were homogeneous, data was analyzed by the Dunnett test, whereas heterogeneous data was analyzed by the Dunnett type mean rank test ($p < 0.05$, two-sided).

In the recovery test, these values of two groups were analyzed by F test. If variances were homogeneous, data was analyzed by the Student t-test, whereas heterogeneous data was analyzed by the Aspin-Welch t-test ($p < 0.05$, two-sided).

Reproductive indices

Each parameter was determined by the following equations:

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

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

Insemination index (%) = (No. of impregnated males / No. of copulated males) × 100

Gestation length (days) = No. of days from pregnancy 0 to delivery 0

Delivery index (%) = (No. of females which delivered liveborns / No. of pregnant females) × 100

Implantation index (%) = (No. of implantation sites / No. of corpora lutea) × 100
Stillborn index (%) = (No. of stillborn / No of liveborns and stillborns) × 100
Live birth index (%) = (No. of liveborn / No. of implantation sites) × 100
External abnormalities (%) = (No. of pups with external abnormalities / No. of liveborns) × 100
Sex ratio = No. of liveborns males / No. of liveborns

Offspring viability indices

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

effects observed, treatment-related

Description (incidence and severity)

See 7.5.1

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

no effects observed

Clinical biochemistry findings

no effects observed

Description (incidence and severity)

Including blood hormones (T3, T4, TSH)

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

Gross pathological findings

effects observed, treatment-related

Description (incidence and severity)

See 7.5.1

Neuropathological findings

not examined

Histopathological findings: non-neoplastic

effects observed, treatment-related

Description (incidence and severity)

See 7.5.1

Histopathological findings: neoplastic

not examined

Reproductive function / performance (P0)**Reproductive function: oestrous cycle**

no effects observed

Reproductive function: sperm measures

not examined

Reproductive performance

no effects observed

Details on results (P0)**1) Estrous Cycle**

There were no animals showing abnormal estrous cycles, and there were no significant differences in the average length of the estrous cycle between the control group and any treatment groups.

2) Results of Mating

There were no significant differences in the incidence of females with irregular estrus cycle, mating period with the number of estrus and day of conceiving, copulation index, and fertility index between the control group and any treatment groups.

3) Delivery Data and Delivery

There were no significant differences in the gestation length, number of corpora lutea, number of implantation sites, implantation index, and delivery index between the control group and any treatment groups.

Body weight and weight changes

See 7.5.1

Organ weight findings

See 7.5.1

Gross pathological findings

See 7.5.1

Histopathological findings

See 7.5.1

Effect levels (P0)

Key result

true

Dose descriptor

NOAEL

Effect level

1000

mg/kg bw/day (actual dose received)

Based on

test mat.

Sex

male/female

Basis for effect level

other: No effects on reproduction

Results: F1 generation

General toxicity (F1)**Clinical signs**

no effects observed

Mortality / viability

no mortality observed

Body weight and weight changes

no effects observed

Gross pathological findings

no effects observed

Effect levels (F1)**Key result**

true

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: No effects on development

Overall reproductive toxicity

Key result

true

Reproductive effects observed

no

Any other information on results incl. tables

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

https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF35948-25-5d.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), there were no effects on reproductive and developmental parameters up to 1000 mg/kg bw/day. The NOAEL for the rat reproductive/developmental toxicity of 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide was regarded as 1000 mg/kg bw/day, the highest dose tested.

Executive summary

A combined repeated-dose toxicity study with the reproduction/developmental toxicity screening test was done according to OECD TG 422. Male and female rats (12 animals/sex/dose) were administered with 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide via oral gavage at doses of 0 [vehicle: corn oil], 100, 300, and 1,000 mg/kg bw/day. Males (12/dose) were then treated with 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide for 42 days, which include a 14-day pre-mating period and a subsequent mating period, while females (12/dose) were treated for 41–46 days, which include a 14-day pre-mating, mating and gestation periods until lactation day 4. Among the 12 males administered with 0 and 1,000 mg/kg bw/day, 5 were assigned as recovery group. Additional 10 females treated with 0 and 1,000 mg/kg bw/day were assigned as a satellite group and treated with 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide for 42 days, with no mating, and examined after a 14-day recovery period.

No effects on reproductive toxicity (fertility and reproductive organs) and developmental toxicity up to the highest dose were recorded. Since the effects were not even observed at 1,000 mg/kg bw/day, the NOAEL for the reproduction and development toxicity was 1,000 mg/kg bw/day in rats.

DOMAIN

SUBSTANCE: 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide

UUID: adb0411e-4315-4747-be09-3ca5483be250

Dossier UUID:

Author: SuperUser

Date: 2020-10-01T12:14:04.934+09:00

Remarks:

Substance name

6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide

Public name

6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide

Legal entity

[National Institute of Health Sciences, Japan](#)

Contact persons

Person

[Hirose, Akihiko; National Institute of Health Sciences](#)

Last name

Hirose

First name

Akihiko

Organisation

National Institute of Health Sciences

Department

Division of Risk Assessment

Title

Dr.

Remarks

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

Identification of substance

Reference substance

[6H-dibenz\[c,e\]\[1,2\]oxaphosphorin 6-oxide / 35948-25-5](#)

EC number

EC name

CAS number

35948-25-5

IUPAC name

CAS name

Role in the supply chain

Manufacturer

false

Importer

false

Only representative

false

Downstream user

false

References

LEGAL_ENTITY: National Institute of Health Sciences, Japan

UUID: 0952b3b9-2d0c-4bc8-925e-b069be7789b7

Dossier UUID:

Author: SuperUser

Date: 2020-02-19T14:42:16.272+09:00

Remarks:

General information

Legal entity name

National Institute of Health Sciences, Japan

REFERENCE_SUBSTANCE: 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide

UUID: 08514a60-3c3a-450d-a41f-2ead8f0631a6

Dossier UUID:

Author: SuperUser

Date: 2019-12-19T11:26:29.000+09:00

Remarks:

General information

Reference substance name

6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide

Reference substance information

Synonyms

Identifier

EC name

Identity

6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide

Identifier

EC number

Identity

252-813-7

CAS information

CAS number

35948-25-5

TEST_MATERIAL_INFORMATION: 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide

UUID: b3f2f291-72fd-45df-b3b7-59d132f039da

Dossier UUID:

Author: SuperUser

Date: 2019-12-19T11:36:43.000+09:00

Remarks:

Name

6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide

LITERATURE: Combined repeated dose toxicity study with the reproductive/developmental toxicity screening test of 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide by oral administration in rats

UUID: 87fb1591-7111-41f5-a1a3-064c2272fdcc

Dossier UUID:

Author: SuperUser

Date: 2020-03-24T10:22:29.000+09:00

Remarks:

General information

Reference Type

study report

Title

Combined repeated dose toxicity study with the reproductive/developmental toxicity screening test of 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide 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/PDF35948-25-5d.pdf

Testing facility

BoZo Research Center

Report no.

R-1050

CONTACT: Hirose, Akihiko; National Institute of Health Sciences

UUID: 4293b0a1-fb1d-47d7-a0f7-2f93622aeb27

Dossier UUID:

Author: SuperUser

Date: 2020-02-20T15:27:47.410+09:00

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

General information

Last name

Hirose

First name

Akihiko

Organisation

National Institute of Health Sciences

Department

Division of Risk Assessment

Title

Dr.

Remarks

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

LITERATURE: In Vitro Chromosomal Aberration Test of 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide on Cultured Chinese Hamster Cells.

UUID: 9ce1f33e-43a6-47e7-9568-b4a6bd2072da

Dossier UUID:

Author: SuperUser

Date: 2020-03-17T15:53:44.000+09:00

Remarks:

General information

Reference Type

study report

Title

In Vitro Chromosomal Aberration Test of 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide on Cultured Chinese Hamster Cells.

Author

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

Bibliographic source

Japan Existing Chemical Data Base (JECDB) https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF35948-25-5f.pdf

Testing facility

Bozo Research Center Inc.

Report no.

M-1406

LITERATURE: Reverse Mutation Test of 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide on Bacteria.

UUID: 174bb4bd-0c13-4e59-9957-9ecac2937682

Dossier UUID:

Author: SuperUser

Date: 2020-03-17T16:05:23.000+09:00

Remarks:

General information

Reference Type

study report

Title

Reverse Mutation Test of 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide on Bacteria.

Author

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

Bibliographic source

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