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**Name:** Tetraphenyltin(IV) / tetraphenylstannane / 595-90-4

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

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**Printing date:** 2019-09-03T16:08:54.793+09:00

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# Tetraphenyltin(IV)

## CORE

### General information

#### Identification

**SUBSTANCE:** Tetraphenyltin(IV)

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**UUID:** 2bcc0ba6-3b8c-49ce-98d1-aec95545fade

**Dossier UUID:**

**Author:** SuperUser

**Date:** 2019-03-27T09:53:09.260+09:00

**Remarks:**

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**Substance name**

Tetraphenyltin(IV)

**Legal entity**

[National Institute of Health Sciences / Kawasaki / Japan](#)

#### Identification of substance

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**Reference substance**

[tetraphenyltin / tetraphenylstannane / 595-90-4 / 209-872-9](#)

**EC number**

209-872-9

**EC name**

EC Inventory

**CAS number**

595-90-4

**CAS name**

**IUPAC name**

tetraphenylstannane

#### Role in the supply chain

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**Manufacturer**

false

**Importer**

false

**Only representative**

false

**Downstream user**

false

# OECD

## Health Effects

### Repeated dose toxicity: oral

ENDPOINT\_STUDY\_RECORD: Repeated dose toxicity: oral.001

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UUID: 4a06e5fb-bede-4840-a3c1-a41af7a2f975

Dossier UUID:

Author: SuperUser

Date: 2019-03-27T09:53:30.164+09:00

Remarks:

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## Administrative data

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### Endpoint

repeated dose toxicity: oral, other

### Type of information

experimental study

### Adequacy of study

key study

### Robust study summary

false

### Used for classification

false

### Used for SDS

false

### Reliability

1 (reliable without restriction)

### Rationale for reliability incl. deficiencies

guideline study

Reliability 1

### Cross-reference

#### Reason / purpose

reference to same study

#### Related information

[OECD / Toxicity to reproduction / Toxicity to reproduction.001 / Tetraphenyltin\(IV\) / tetraphenylstannane / 595-90-4](#)

## Data source

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### Reference

[A combined repeated dose/reproductive developmental toxicity study of tetraphenyltin by oral adminis... / Ministry of Health, Labor and Welfare, Japan / study report](#)

**Data access**

data published

## Materials and methods

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### 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

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### Specific details on test material used for the study

- Name of test material (as cited in study report): Tetraphenyltin
- Analytical purity: 97.9%
- Storage condition of test material: at a cold (temperature 2-6°C) and dark place, with airtight stopper.
- Stability under test conditions: The stability of test material was identified by analysis of the remainder.

## Test animals

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### Species

rat

common rodent species

### Strain

other: CrI: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 388 g (357-421 g), female 243 g (213-278 g)
- Housing: Animals were individually housed in bracket-type metallic wire-mesh cages (265W × 426D × 200H mm), Dams were bred individually or with individual littermates in polycarbonate cages with flat floors (265W x 426D x 200H mm) and standard bedding.
- Diet: Solid feed (MR stock: Nosan Corporation) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation period: 14 days

#### ENVIRONMENTAL CONDITIONS

- Temperature (°C): 22±3 (actual temperature: 20.7-24.9°C)

- Humidity (%): 55±10% (actual humidity: 45-63%)
- Air changes (per hr): >10
- Photoperiod (hrs dark / hrs light): 12 hr dark/12 hr light (light: 7:00~19:00)

## Administration / exposure

### Route of administration

oral: gavage

### Vehicle

olive oil

### Details on oral exposure

- Amount of vehicle (if gavage): 5 mL/kg
- Dosing volume: 5 mL/kg

### Analytical verification of doses or concentrations

yes

### Duration of treatment / exposure

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

(P) Females: 42-54 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

<b>Dose / conc.</b>	
0	mg/kg bw/day (actual dose received)
<b>Dose / conc.</b>	
4	mg/kg bw/day (actual dose received)
<b>Dose / conc.</b>	
20	mg/kg bw/day (actual dose received)
<b>Dose / conc.</b>	
100	mg/kg bw/day (actual dose received)
<b>Dose / conc.</b>	
500	mg/kg bw/day (actual dose received)

### No. of animals per sex per dose

Main group: 12 animals/sex/dose

Satellite (Recovery) group: 5 males/dose and 5 females/dose (0 and 500 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 500 mg/kg bw/day was selected as an expected obvious toxic dose, and the lowest dose of 4 mg/kg bw/day was selected as an expected no toxic dose. The middle dose levels of 20 and 100 mg/kg bw/day were selected.

- Rationale for animal assignment (if not random): Body weight-balanced randomization [14-day preliminary study]

Study 1:

A 14-day repeated dose oral toxicity test (CrI:CD(SD) rats, doses: 0 (olive oil), 50, 100, 200, 500 or 1000 mg/kg bw/day). At 50 mg/kg bw/day or more, treatment related effects were observed. High value of ALT were observed in males 1000 mg/kg bw/day.

Study 2:

A 14-day repeated dose oral toxicity test (CrI:CD(SD) rats, doses: 0 (olive oil), 1.5, 3, 6, 12.5, 25 or 50 mg/kg bw/day). Increase in relative liver weights were observed in males at 3 mg/kg bw/day, females at 6 mg/kg bw/day and 25 mg/kg bw/day or more.

## **Examinations**

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### **Observations and examinations performed and frequency**

CAGE SIDE OBSERVATIONS: Yes

- Time schedule: 3 times/day (am: before and after administration; pm) during the administration period. 2 times/day (am and pm) during the recovery period.

DETAILED CLINICAL OBSERVATIONS: Yes

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

BODY WEIGHT: Yes

- Time schedule for examinations:

Males were weighed on Day 1, 7, 14, 21, 28, 35, and 42 of administration, and weighed on Day 7 and 14 of recovery.

Female satellite groups were weighed same frequencies to male recovery groups.

Females in the main groups were weighed on Day 1, 7 and 14 of administration and copulated female s were weighed on Day 0, 7, 14 and 20 of gestation, and days 0 and 4 of lactation.

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 recovery groups; on Day 1, 7, 14, 21, 28, 35, and 41 of administration, and on Day 7 and 13 of recovery.

Female satellite groups were weighed same frequencies to male recovery groups.

Females in the main group; on Day 1, 7 and 14 of administration and copulated females were weighed on Day 0, 7, 14 and 20 of gestation, and days 0 and 3 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: 5 animals/sex/group

- Parameters examined included RBC, hemoglobin, hematocrit, MCV, MCH, MCHC, platelet, reticulocyte, PT, APTT, WBC and differential WBC.

**CLINICAL CHEMISTRY: Yes**

- Time schedule for collection of blood: 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 examined included total protein, albumin, A/G ratio, total bilirubin, glucose, total cholesterol, triglyceride, phospholipid, AST, ALT, LDH, ChE, ALP, gamma-GTP, BUN, creatinine, Na, K, Cl, Ca and IP.

**URINALYSIS OF MALES: Yes**

- Time schedule for collection of urine (male only): On Day 37 of administration, and on Day 9 of recovery.
- Metabolism cages used for collection of urine: Yes
- How many animals: 5 animals/group
- Parameters examined included color, cloudy, urine volume, specific gravity, pH, protein, glucose, ketone body, bilirubin, occult blood and urobilinogen.

**NEUROBEHAVIOURAL EXAMINATION: Yes**

- Time schedule for examinations: On week 6 of the administration period, and on week 2 of the recovery period
- Dose groups that were examined: All dose groups (5 animals/sex/group)
- Battery of functions tested: sensory activity (hearing reaction, eye sight reaction, sense of touch reaction, pain reaction, pupil reflex, righting reflex), grip strength, motor activity

**Sacrifice and pathology**

**GROSS PATHOLOGY: Yes**

ORGAN WEIGHT: Yes [brain, thymus, heart, liver, kidney, adrenal gland, spleen, seminal vesicle, testis, epididymis, pituitary, thyroid]

HISTOPATHOLOGY: Yes, [brain, pituitary, spinal cord, thyroid, parathyroid, heart, thymus, trachea, lung, liver, kidney, adrenal, spleen, stomach, small intestine, large intestine, sciatic nerve, bone, bone marrow, lymph nodes (mesenteric and cervical lymph nodes), urinary bladder, testis, seminal vesicle, prostate, epididymis, mammary gland, ovary and uterus.]

**Statistics**

As for parametric data (grip strength, locomotor activity, body weight, body weight gain, food consumption, hematology and clinical chemistry data, organ weights, quantitative urinalysis data, number of corpora lutea, number of implantation sites, number of pups born, number of pups alive, number of stillborn), the values of means and standard deviations were calculated per group. When more than three groups exist in the test group, Bartlett test for variance was done, and if the variance was homogenous, ANOVA was applied. If the variance was not homogenous or data was non-parametric (differential WBC percentage, qualitative urinalysis data, stages of spermatogenesis, length of the estrous cycle, implantation index, delivery index, live birth index, viability index.), Kruskal-Wallis rank sum test was used. Consequently, if the result was significant, Dunnett multiple comparison or Dunnett typed method was used for detection of statistical significance against control group. When the number of the test group was two, F-test was used as for parametric data.

Then, student's t-test or Aspin-Welch's t-test was applied depending on the result of homogeneity of variance. While, as for non-parametric data, Man-Whitney's U-test was applied. Furthermore, as for categorized data (incidence of abnormal findings in clinical observation, detailed observation, sensory functional examination, necropsy and histopathology, copulation index, fertility index, gestation index), Fischer's exact test was used. In the histopathological examination findings, Mann-Whitney's U test was used for graded data, and chi-squared test was used for sex ratio of pups. In any tests, level of significance was set at 5%.

**Results and discussion**

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## Results of examinations

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### **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**

no effects observed

### **Clinical biochemistry findings**

no effects observed

### **Urinalysis findings**

no effects observed

### **Behaviour (functional findings)**

no effects observed

### **Organ weight findings including organ / body weight ratios**

no effects observed

### **Gross pathological findings**

no effects observed

### **Histopathological findings: non-neoplastic**

no effects observed

### **Histopathological findings: neoplastic**

not examined

### **Details on results**

CLINICAL SIGNS AND MORTALITY:

Mortality: There was no death.

Clinical signs: There were no effects related to the test substance.

DETAILED CLINICAL OBSERVATIONS, MANIPULATIVE TEST, GRIP STRENGTH TEST AND LOCOMOTOR ACTIVITY MEASUREMENT: There were no changes related to the test substance.

BODY WEIGHT:

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

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

URINALYSIS: 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:

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

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

ORGAN WEIGHTS:

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

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

HISTOPATHOLOGY: NON-NEOPLASTIC:

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

## Effect levels

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<b>Key result</b> true
<b>Dose descriptor</b> NOAEL
<b>Effect level</b>  500 mg/kg bw/day (actual dose received)
<b>Based on</b> test mat.
<b>Sex</b> male/female
<b>Basis for effect level</b> other: There were no effects related to the test substance.

## Any other information on results incl. tables

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

[http://dra4.nihs.go.jp/mhlw\\_data/home/pdf/PDF595-90-4d.pdf](http://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF595-90-4d.pdf)

## Applicant's summary and conclusion

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### Executive summary

The combination of a study of repeated-oral-dose toxicity and a reproduction/developmental toxicitiescreening test was performed in accordance with OECD TG 422. Tetraphenyltin (IV) was

administered to male and female rats (12 animals/sex/dose) at 0 (vehicle: olive oil), 4, 20, 100, and 500 mg/kg bw/day. The males were dosed for 42 days, including a 14-day pre-mating period and a subsequent mating period. The females were dosed for 42–54 days, including 14-day pre-mating, mating, and gestation periods and until lactation day 4. Of the 12 males in the control and 500 mg/kg bw/day groups, 5 were treated as a recovery group. Additionally, five females per dose were administered the test substance at 0 and 500 mg/kg bw/day for 42 days without mating; they were examined after a 14-day recovery period (satellite group).

No adverse effects were observed in clinical characteristics, FOB, body weight, food consumption, urinalysis, hematology, clinical biochemistry, organ weight, or pathology after the administration and recovery periods for any of the treated groups. In a 14-day preliminary study of tetraphenyltin (IV) in rats, relative liver weights were found to increase by 3 to 1,000 mg/kg bw/day in males and by 6 to 1,000 mg/kg bw/day in females. For this reason, the largest dose tested in this main study was expected to cause overt toxicity. No clear reason was adduced why no adverse effects on the liver were observed in this study, but age at necropsy and duration of administration might each have affected the response. These data indicate that the NOAEL of repeated-dose toxicity for tetraphenyltin (IV) should be estimated to be 500 mg/kg bw/day (the highest dose tested).

## Genetic toxicity in vitro

### ENDPOINT\_STUDY\_RECORD: Genetic toxicity in vitro.001

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**UUID:** 185693f0-194e-44c0-b530-3d7fd8644326

**Dossier UUID:**

**Author:** SuperUser

**Date:** 2019-02-15T15:08:37.427+09:00

**Remarks:**

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## Administrative data

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### Endpoint

in vitro gene mutation study in bacteria

### Type of information

experimental study

### Adequacy of study

key study

### Robust study summary

true

### Used for classification

false

### Used for SDS

false

### Reliability

1 (reliable without restriction)

### Rationale for reliability incl. deficiencies

guideline study

Reliability 1

## Data source

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### Reference

[Reverse Mutation Test of Tetraphenyltin\(IV\) / Ministry of Health, Labour and Welfare \(MHLW\), Japan / study report](#)

### Data access

data published

## Materials and methods

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### Test guideline

#### Qualifier

according to

#### Guideline

OECD Guideline 471 (Bacterial Reverse Mutation Assay)

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in vitro gene mutation study in bacteria

**GLP compliance**

yes

**Test material**

**Specific details on test material used for the study**

- Lot No.: EWJ4190
- Purity: 99%
- Solubility: insoluble in water, DMSO, acetone, N,N-dimethylformamide, 1,4-dioxane, and tetrahydrofuran
- Physical state: white powder
- Storage condition of test material: room temperature (16-28 degree C)

**Method**

**Species / strain**

**Species / strain**

S. typhimurium TA 1535, TA 1537, TA 98, TA 100 and E. coli WP2  
bacteria

**Metabolic activation**

with and without

**Metabolic activation system**

S9 mix: Rat liver, induced with phenobarbital and 5,6-benzoflavone

**Test concentrations with justification for top dose**

Dosage of each strain with or without S9

+/-S9 mix: 0, 19.5, 39.1, 78.1, 156, 313 µg /plate

Maximum concentration was established based on the result of the preliminary test at concentration up to 5000 ug/plate. In this test, growth inhibition was not observed, but precipitation was observed at 313-5000 µg/plate for all strains with and without S9 mix.

**Vehicle**

Water (suspended)

**Controls**

**Negative controls**

no

**Solvent controls**

yes

**True negative controls**

no

**Positive controls**

yes

**Positive control substance**

sodium azide

- S9 mix (TA 1535)

benzo(a)pyrene

+S9 mix (TA100, TA98, TA1537)  
other: see Remarks

**Remarks**

without S9 mix:2-(2-Furyl)-3-(5-nitro -2-furyl)acrylamide (TA100, TA98, WP2uvrA), without S9 mix:  
2-Methoxy-6-chloro-9-[3-(2-chloroethyl) aminopropylamino]acridine-2HCl (TA1537) with S9 mix: 2-  
aminoanthracene (TA 1535, WP2uvrA)

**Details on test system and conditions**

METHOD OF APPLICATION: Preincubation

DURATION- Preincubation period: 20 min at 37°C

- Exposure duration:48 hrs

NUMBER OF PLATES: 3

NUMBER OF REPLICATIONS: 2

DETERMINATION OF CYTOTOXICITY- Method: other: growth inhibition

**Evaluation criteria**

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

**Statistics**

not used

## Results and discussion

**Test results**

**Key result**

true

**Species / strain**

S. typhimurium TA 1535  
bacteria

**Metabolic activation**

with and without

**Genotoxicity**

negative

**Cytotoxicity**

no, but tested up to limit concentrations

**Vehicle controls valid**

yes

**Positive controls valid**

yes

**Key result**

true

**Species / strain**

S. typhimurium TA 1537  
bacteria

**Metabolic activation**

with and without

**Genotoxicity**

negative

**Cytotoxicity**

no, but tested up to limit concentrations

**Vehicle controls valid**

yes

**Positive controls valid**

yes

**Key result**

true

**Species / strain**

S. typhimurium TA 98

bacteria

**Metabolic activation**

with and without

**Genotoxicity**

negative

**Cytotoxicity**

no, but tested up to limit concentrations

**Vehicle controls valid**

yes

**Positive controls valid**

yes

**Key result**

true

**Species / strain**

S. typhimurium TA 100

bacteria

**Metabolic activation**

with and without

**Genotoxicity**

negative

**Cytotoxicity**

no, but tested up to limit concentrations Precipitation was observed at 313 µg /plate.

**Vehicle controls valid**

yes

**Positive controls valid**

yes

**Key result**

true

**Species / strain**

E. coli WP2 uvr A pKM 101

bacteria

**Metabolic activation**

with and without

**Genotoxicity**

negative

**Cytotoxicity**

no, but tested up to precipitating concentrations

**Vehicle controls valid**

yes

**Positive controls valid**

yes

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## Applicant's summary and conclusion

### Conclusions

With metabolic activation: Negative

Without metabolic activation: Negative

### Executive summary

In a bacterial reverse mutation assay using *S. typhimurium* TA100, TA1535, TA98, and TA1537, and *E. coli* WP2uvrA/pKM101 (OECD TG 471), negative results were obtained for tetraphenyltin(IV) with or without metabolic activation.



## ENDPOINT\_STUDY\_RECORD: Genetic toxicity in vitro.002

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**UUID:** c4b9729b-d2a6-4818-baa4-c844c57812c2

**Dossier UUID:**

**Author:** SuperUser

**Date:** 2019-02-15T15:38:46.345+09:00

**Remarks:**

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## Administrative data

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### Endpoint

in vitro cytogenicity / chromosome aberration study in mammalian cells

### Type of information

experimental study

### Adequacy of study

key study

### Robust study summary

true

### Used for classification

false

### Used for SDS

false

### Reliability

1 (reliable without restriction)

### Rationale for reliability incl. deficiencies

guideline study

Reliability 1

## Data source

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### Reference

[In Vitro Chromosomal Aberration Test of Tetraphenyltin\(IV\) on Cultured Chinese Hamster Cells / Ministry of Health, Labour and Welfare \(MHLW\), Japan / study report](#)

### Data access

data published

## Materials and methods

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### Test guideline

#### Qualifier

according to

#### Guideline

OECD Guideline 473 (In Vitro Mammalian Chromosome Aberration Test)

in vitro cytogenicity / chromosome aberration study in mammalian cells

### GLP compliance

yes

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## Test material

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### Specific details on test material used for the study

- Lot No.: EWJ4190
- Purity: 99%
- Solubility: insoluble in water, suspend in DMSO
- Physical state: white powder
- Storage condition of test material: room temperature (15-24 degree C)

## Method

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### Species / strain

#### Species / strain

other:

#### Details on mammalian cell lines (if applicable)

Chinese hamster lung(CHL/IU) cell

#### Metabolic activation

with and without

#### Metabolic activation system

S9 mix: Rat liver, induced with phenobarbital and 5,6- benzoflavone

### Test concentrations with justification for top dose

Short-term treatment(+S9 mix): 0, 134.4, 268.8, 537.5, 1075, 2150 µg/mL

Confirmation test: 1200, 1400, 1600, 1800, 2000 µg/mL

Short-term treatment(-S9 mix): 0, 16.8, 33.59, 67.19, 134.4 µg/mL

Confirmation test:80, 90, 100, 110, 120 µg/mL

Cell-growth inhibition test was conducted up to the limited concentration of 4300 µg/mL (10 mM)

Cell growth inhibition (>50%) was observed for short-term treatment at 1075 µg/mL (+S9 mix) and 134.4 µg/mL (-S9mix), and continuous treatment at 67.19 µg/mL (24h) and 33.59 µg/mL (48h).

### Vehicle

DMSO

### Controls

#### Negative controls

no

#### Solvent controls

yes

#### True negative controls

no

#### Positive controls

yes

#### Positive control substance

cyclophosphamide

(with S9 mix)

mitomycin C

(without S9 mix)

### Details on test system and conditions

METHOD OF APPLICATION: Exposure duration: [short-term treatment]:6 h + 18 h, [continuous treatment]: 24h and 48h

NUMBER OF CELLS EVALUATED: 200 cells /concentration (100 cells/plate x 2)

Plates/test: 2

### Evaluation criteria

For the evaluation of the frequencies of structural aberrations and of polyploidy induced, the following criteria were employed. Appearance incidence of cell with chromosomal aberrations: Negative(-): less than 5%, Equivocal(±): 5% or more and less than 10%, Positive(+): 10% or more

### Statistics

not used

## Results and discussion

---

### Test results

**Key result**

true

**Species / strain**

other: Chinese hamster lung(CHL/IU) cells

**Metabolic activation**

with and without

**Genotoxicity**

positive

**Cytotoxicity**

yes at 2000 µg/mL and higher with S9 mix, at 134.4 µg/mL without S9 mix

**Vehicle controls valid**

yes

**Positive controls valid**

yes

### Additional information on results

In the confirmation tests, Tetraphenyltin(IV) induced structural aberrations with and without S9 mix. Incidence of structural aberrations were 2.0%, 3.5%, 17.5%, and 52.5 % at 1200, 1400, 1600, and 1800 µg/mL with S9 mix, and 0.5%, 1.0%, 0.5%, 6.5%, and 11.0% at 80, 90, 100, 110, and 120 µg/mL without S9mix. Polyploidy was not observed in any test conditions. Positive and vehicle control groups were valid.

## Any other information on results incl. tables

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

[http://dra4.nihs.go.jp/mhlw\\_data/home/pdf/PDF595-90-4f.pdf](http://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF595-90-4f.pdf)

## Applicant's summary and conclusion

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### Conclusions

Tetraphenyltin(IV) induced structural aberrations with and without S9 mix

**Executive summary**

In an in vitro chromosomal aberration test using CHL/IU cells (OECD TG 473), positive results were obtained with or without metabolic activation.

## Toxicity to reproduction

### ENDPOINT\_STUDY\_RECORD: Toxicity to reproduction.001

---

**UUID:** e2e5b6da-25b9-460d-a293-2213b468e32f

**Dossier UUID:**

**Author:** SuperUser

**Date:** 2019-03-27T09:53:30.196+09:00

**Remarks:**

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## Administrative data

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### 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

reference to same study

#### Related information

[OECD / Repeated dose toxicity: oral / Repeated dose toxicity: oral.001 / Tetraphenyltin\(IV\) / tetraphenylstannane / 595-90-4](#)

## Data source

---

### Reference

[A combined repeated dose/reproductive developmental toxicity study of tetraphenyltin by oral adminis... / Ministry of Health, Labor and Welfare, Japan / study report](#)

### Data access

data published

## Materials and methods

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### 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

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**Specific details on test material used for the study**

- Name of test material (as cited in study report): Tetraphenyltin
- Analytical purity: 97.9%
- Storage condition of test material: at a cold (temperature 2-6°C) and dark place, with airtight stopper.
- Stability under test conditions: The stability of test material was identified by analysis of the remainder.

### Test animals

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**Species**

rat

**Strain**

other: CrI: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 388 g (357-421 g), female 243 g (213-278 g)
- Housing: Animals were individually housed in bracket-type metallic wire-mesh cages (265W × 426D × 200H mm), Dams were bred individually or with individual littermates in polycarbonate cages with flat floors (265W x 426D x 200H mm) and standard bedding.
- Diet: Solid feed (MR stock: Nosan Corporation) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation period: 12 days

**ENVIRONMENTAL CONDITIONS**

- Temperature (°C): 22±3 (actual temperature: 20.7-24.9°C)
- Humidity (%): 55±10% (actual humidity: 45-63%)
- Air changes (per hr): >10
- Photoperiod (hrs dark / hrs light): 12 hr dark/12 hr light (light: 7:00~19:00)

### Administration / exposure

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**Route of administration**

oral: gavage

**Vehicle**

olive oil

**Details on exposure**

- Amount of vehicle (if gavage): 5 mL/kg
- Dosing volume: 5 mL/kg

**Analytical verification of doses or concentrations**

yes

**Duration of treatment / exposure**

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

(P) Females: 42-54 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**

<b>Dose / conc.</b>	
0	mg/kg bw/day (actual dose received)
<b>Dose / conc.</b>	
4	mg/kg bw/day (actual dose received)
<b>Dose / conc.</b>	
20	mg/kg bw/day (actual dose received)
<b>Dose / conc.</b>	
100	mg/kg bw/day (actual dose received)
<b>Dose / conc.</b>	
500	mg/kg bw/day (actual dose received)

**No. of animals per sex per dose**

Main group: 12 animals/sex/dose

Satellite (Recovery) group: 5 males/dose and 5 females/dose (0 and 500 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 500 mg/kg bw/day was selected as an expected obvious toxic dose, and the lowest dose of 4 mg/kg bw/day was selected as an expected no toxic dose. The middle dose levels of 20 and 100 mg/kg bw/day were selected.
- Rationale for animal assignment (if not random): Body weight-balanced randomization

[14-day preliminary study]

Study 1:

A 14-day repeated dose oral toxicity test (CrI:CD(SD) rats, doses: 0 (olive oil), 50, 100, 200, 500 or 1000 mg/kg bw/day). At 50 mg/kg bw/day or more, treatment related effects were observed. High value of ALT were observed in males 1000 mg/kg bw/day.

Study 2:

A 14-day repeated dose oral toxicity test (CrI:CD(SD) rats, doses: 0 (olive oil), 1.5, 3, 6, 12.5, 25 or 50 mg/kg bw/day). Increase in relative liver weights were observed in males at 3 mg/kg bw/day, females at 6 mg/kg bw/day and 25 mg/kg bw/day or more.

## Examinations

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### Parental animals: Observations and examinations

CAGE SIDE OBSERVATIONS: Yes

- Time schedule: 3 times/day (am: before and after administration; pm) during the administration period. 2 times/day (am and pm) during the recovery period.

DETAILED CLINICAL OBSERVATIONS: Yes

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

BODY WEIGHT: Yes

- Time schedule for examinations:

Males were weighed on Day 1, 7, 14, 21, 28, 35, and 42 of administration, and weighed on Day 7 and 14 of recovery.

Female satellite groups were weighed same frequencies to male recovery groups.

Females in the main groups were weighed on Day 1, 7 and 14 of administration and copulated females were weighed on Day 0, 7, 14 and 20 of gestation, and days 0 and 4 of lactation.

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 recovery groups; on Day 1, 7, 14, 21, 28, 35, and 41 of administration, and on Day 7 and 13 of recovery.

Female satellite groups were weighed same frequencies to male recovery groups.

Females in the main group; on Day 1, 7 and 14 of administration and copulated females were weighed on Day 0, 7, 14 and 20 of gestation, and days 0 and 3 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: 5 animals/sex/group

- Parameters examined included RBC, hemoglobin, hematocrit, MCV, MCH, MCHC, platelet, reticulocyte, PT, APTT, WBC and differential WBC.

CLINICAL CHEMISTRY: Yes

- Time schedule for collection of blood: 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 examined included total protein, albumin, A/G ratio, total bilirubin, glucose, total cholesterol, triglyceride, phospholipid, AST, ALT, LDH, ChE, ALP, gamma-GTP, BUN, creatinine, Na, K, Cl, Ca and IP.



**URINALYSIS OF MALES: Yes**

- Time schedule for collection of urine (male only): On Day 37 of administration, and on Day 9 of recovery.
- Metabolism cages used for collection of urine: Yes
- How many animals: 5 animals/group
- Parameters examined included color, cloudy, urine volume, specific gravity, pH, protein, glucose, ketone body, bilirubin, occult blood and urobilinogen.

**NEUROBEHAVIOURAL EXAMINATION: Yes**

- Time schedule for examinations: On week 6 of the administration period, and on week 2 of the recovery period
- Dose groups that were examined: All dose groups (5 animals/sex/group)
- Battery of functions tested: sensory activity (hearing reaction, eye sight reaction, sense of touch reaction, pain reaction, pupil reflex, righting reflex), grip strength, motor activity

**Estrous 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.

**Sperm parameters (parental animals)**

Parameters examined in all P male parental generations: testis weight, epididymis weight, histopathological examinations for testes, epididymides, seminal vesicle including coagulating gland 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, weight gain, physical or behavioral abnormalities.

**Postmortem examinations (parental animals)**

METHOD OF SACRIFICED: All animals were sacrificed by exsanguination under ether anesthesia.

SACRIFICE: Male animals: On Day 42, Maternal animals: on Day 5 of lactation, and Male recovery and female satellite animals: on next Day 14 of recovery.

**GROSS PATHOLOGY: Yes**

ORGAN WEIGHT: Yes [brain, thymus, heart, liver, kidney, adrenal gland, spleen, seminal vesicle, testis, epididymis, pituitary, thyroid]

HISTOPATHOLOGY: Yes, [brain, pituitary, spinal cord, thyroid, parathyroid, heart, thymus, trachea, lung, liver, kidney, adrenal, spleen, stomach, small intestine, large intestine, sciatic nerve, bone, bone marrow, lymph nodes (mesenteric and cervical lymph nodes), urinary bladder, testis, seminal vesicle, prostate, epididymis, mammary gland, ovary and uterus.]

**Postmortem examinations (offspring)**

**SACRIFICE**

- The F1 offspring were sacrificed at 4 days of age.

**GROSS NECROPSY**

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

**HISTOPATHOLOGY / ORGAN WEIGHTS**

- Not examined.

**Statistics**

As for parametric data (grip strength, locomotor activity, body weight, body weight gain, food consumption, hematology and clinical chemistry data, organ weights, quantitative urinalysis data, number

of corpora lutea, number of implantation sites, number of pups born, number of pups alive, number of stillborn), the values of means and standard deviations were calculated per group. When more than three groups exist in the test group, Bartlett test for variance was done, and if the variance was homogenous, ANOVA was applied. If the variance was not homogenous or data was non-parametric (differential WBC percentage, qualitative urinalysis data, stages of spermatogenesis, length of the estrous cycle, implantation index, delivery index, live birth index, viability index,), Kruskal-Wallis rank sum test was used. Consequently, if the result was significant, Dunnett multiple comparison or Dunnett typed method was used for detection of statistical significance against control group. When the number of the test group was two, F-test was used as for parametric data.

Then, student's t-test or Aspin-Welch's t-test was applied depending on the result of homogeneity of variance. While, as for non-parametric data, Man-Whitney's U-test was applied. Furthermore, as for categorized data (incidence of abnormal findings in clinical observation, detailed observation, sensory functional examination, necropsy and histopathology, copulation index, fertility index, gestation index), Fischer's exact test was used. In the histopathological examination findings, Mann-Whitney's U test was used for graded data, and chi-squared test was used for sex ratio of pups. In any tests, level of significance was set at 5%.

### **Reproductive indices**

Estrous cycle: Mean days from metestrus I (III) to next III.

Copulation index (%) = (No. of pairs with successful copulation/No. of pairs mated) × 100

Fertility index (%) = (No. of pregnant females/No. of pairs with successful copulation) × 100

Gestation index (%) = (No. of females with live pups/No. of pregnant females) × 100

Implantation index (%) = (No. of implantation sites/No. of corpora lutea) × 100

Delivery index (%) = (No. of pups born/No. of implantation sites) × 100

Live birth index (%) = (No. of live pups on day 0/No. of pups born) × 100

Sex ratio = Total number of male pups/Total number of female pups

### **Offspring viability indices**

Viability index (%) = (No. of live pups on day 4/No. of live pups on day 0) × 100

## **Results and discussion**

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### **Results: P0 (first parental animals)**

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#### **General toxicity (P0)**

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##### **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**

no effects observed

**Clinical biochemistry findings**

no effects observed

**Urinalysis findings**

no effects observed

**Behaviour (functional findings)**

no effects observed

**Immunological findings**

not examined

**Organ weight findings including organ / body weight ratios**

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: estrous cycle**

no effects observed

**Reproductive function: sperm measures**

no effects observed

**Reproductive performance**

no effects observed

**Effect levels (P0)** \_\_\_\_\_

**Key result**

true

**Dose descriptor**

NOAEL

**Effect level**

500

mg/kg bw/day (actual dose received)

**Based on**

test mat.

**Sex**

male/female

**Basis for effect level**

other: No effects on reproduction

**Results: F1 generation** \_\_\_\_\_

## General toxicity (F1)

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### 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

500

mg/kg bw/day (actual dose received)

### Based on

test mat.

### Sex

male/female

### Basis for effect level

other: No effects on development

## Any other information on results incl. tables

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

[http://dra4.nihs.go.jp/mhlw\\_data/home/pdf/PDF595-90-4d.pdf](http://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF595-90-4d.pdf)

## Applicant's summary and conclusion

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### Executive summary

In the above-described OECD TG 422 study, no effects were observed for reproduction or development. The NOAEL for rat reproduction/developmental toxicity of tetraphenyltin was estimated to be 500 mg/kg bw/day (the highest dose tested).

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# References

## LITERATURE: A combined repeated dose/ reproductive developmental toxicity study of tetraphenyltin by oral administration in rats.

---

**UUID:** 1af8d23f-8a61-4114-8149-fa5d07a694a6

**Dossier UUID:**

**Author:** SuperUser

**Date:** 2019-03-22T10:28:19.000+09:00

**Remarks:**

---

## General information

---

**Reference Type**

study report

**Title**

A combined repeated dose/reproductive developmental toxicity study of tetraphenyltin by oral administration in rats.

**Author**

Ministry of Health, Labor and Welfare, Japan

**Bibliographic source**

Japan Existing Chemical Data Base (JCDB)

**Testing facility**

Research institute for animal science in biochemistry and toxicology (RIAS)

**Report no.**

07-110

# LITERATURE: In Vitro Chromosomal Aberration Test of Tetraphenyltin(IV) on Cultured Chinese Hamster Cells

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**UUID:** 878c6213-6342-4ca1-99a3-7563daf9e0ca

**Dossier UUID:**

**Author:** SuperUser

**Date:** 2019-02-15T15:12:31.092+09:00

**Remarks:**

---

## General information

---

**Reference Type**

study report

**Title**

In Vitro Chromosomal Aberration Test of Tetraphenyltin(IV) on Cultured Chinese Hamster Cells

**Author**

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

**Bibliographic source**

[http://dra4.nihs.go.jp/mhlw\\_data/jsp/SearchPageENG.jsp](http://dra4.nihs.go.jp/mhlw_data/jsp/SearchPageENG.jsp)

**Testing facility**

BoZo Research Center

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# LEGAL\_ENTITY: National Institute of Health Sciences

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

**Dossier UUID:**

**Author:** SuperUser

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

**Remarks:** Disclaimer: The contents in this document were created based on the MHLW (Ministry of Health, Labour and Welfare) peer reviewed study reports (in Japanese) in JECDB (Japan Existing Chemical Database) at [http://dra4.nihs.go.jp/mhlw\\_data/jsp/SearchPageENG.jsp](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.

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## General information

---

### Legal entity name

National Institute of Health Sciences

### Remarks

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

## Identifiers

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### Other IT system identifiers

<b>IT system</b> LEO
<b>ID</b> 10767
<b>IT system</b> IUCLID4
<b>ID</b> 16558402024DIV750

## Contact information

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### Contact address

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**Region / State**

Kanagawa

**Country**

Japan

**Contact persons**

**Person**

Hirose, Akihiko; National Institute of Health Sciences, Japan

**Last name**

Hirose

**First name**

Akihiko

**Organisation**

National Institute of Health Sciences, Japan

**Department**

Division of Risk Assessment

**Title**

Dr

**Country**

Japan



# LITERATURE: Reverse Mutation Test of Tetraphenyltin(IV)

---

**UUID:** 61c00801-5ba2-4de0-a22c-287d1168673f

**Dossier UUID:**

**Author:** SuperUser

**Date:** 2019-02-15T14:51:16.555+09:00

**Remarks:**

---

## General information

---

**Reference Type**

study report

**Title**

Reverse Mutation Test of Tetraphenyltin(IV)

**Author**

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

**Bibliographic source**

[http://dra4.nihs.go.jp/mhlw\\_data/jsp/SearchPageENG.jsp](http://dra4.nihs.go.jp/mhlw_data/jsp/SearchPageENG.jsp)

**Testing facility**

BoZo Research Center

---

# REFERENCE\_SUBSTANCE: tetraphenyltin

---

**UUID:** ECB5-45d3e092-7d22-496f-9a88-14707a9fbb48

**Dossier UUID:**

**Author:** SuperUser

**Date:** 2007-05-10T18:00:00.000+09:00

**Remarks:**

---

## General information

---

**Reference substance name**

tetraphenyltin

## Inventory

---

**Inventory name**

tetraphenyltin

**Inventory**

EC

**Inventory number**

209-872-9

**CAS number**

595-90-4

**Molecular formula**

C<sub>24</sub>H<sub>20</sub>Sn

**Description**

## Reference substance information

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**IUPAC name**

tetraphenylstannane

**Synonyms**

<b>Identity</b>
Stannane, tetraphenyl-
<b>Identity</b>
Stannane, tetraphenyl-
<b>Identity</b>
Stannane, tetraphenyl-

## CAS information

---

**CAS number**

595-90-4

---

## Related substances

---

### Group / category information

DSL Category: Organometallics

USEPA Category: Organotin

## Molecular and structural information

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### Molecular formula

C<sub>24</sub>H<sub>20</sub>Sn

### Molecular weight

427.1256

### SMILES notation

c1ccc(cc1)[Sn](c2ccccc2)(c3ccccc3)c4ccccc4

### InChI

InChI=1/4C6H5.Sn/c4\*1-2-4-6-5-3-1;/h4\*1-5H;/rC24H20Sn/c1-5-13-21(14-6-1)25(22-15-7-2-8-16-22,23-17-9-3-10-18-23)24-19-11-4-12-20-24/h1-20H

### Structural formula

