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**Name:** COMPLETE / SUBSTANCE : 4-sec-Butyl-2,6-di-tert-butylphenol / 4-sec-butyl-2,6-di-tert-butylphenol / 17540-75-9 Fri, 16 Dec 2022, 14:48:49+0900 /

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**Legal entity owner:** National Institute of Health Sciences

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**Printing date:** 2022-12-16T14:48:49.464+09:00

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## Table of Contents

|  |    |
|--|----|
| 0/0 .....  | 1  |
| National Institute of Health Science .....   | 2  |
| 4-sec-Butyl-2,6-di-tert-butylphenol .....  | 3  |
| CORE .....   | 3  |
| 1 General information .....  | 3  |
| 1.10 Assessment approach (assessment entities) .....   | 3  |
| Assessment approach (assessment entities) .....  | 3  |
| OECD .....   | 4  |
| D Health Effects .....   | 4  |
| 67 Repeated dose toxicity: oral .....  | 4  |
| Repeated dose toxicity: oral.001 .....   | 4  |
| 70 Genetic toxicity in vitro .....   | 12 |
| Genetic toxicity in vitro.001 .....  | 12 |
| Genetic toxicity in vitro.002 .....  | 16 |
| 73 Toxicity to reproduction .....  | 20 |
| Toxicity to reproduction.001 .....   | 20 |
| DOMAIN .....   | 29 |
| Substance .....  | 29 |
| Substance .....  | 29 |
| References .....   | 30 |
| Reference Substances .....   | 30 |
| 4-sec-butyl-2,6-di-tert-butylphenol .....  | 30 |
| Test Materials .....   | 32 |
| 4-sec-butyl-2,6-di-tert-butylphenol .....  | 32 |
| Literatures .....  | 33 |
| In Vitro Chromosomal Aberration Test of 4-sec-butyl-2,6-di-tert-butylphenol<br>on Cultured Chinese Hamster Cells. .... | 33 |
| Reproduction/Developmental Toxicity Screening Test on 4-sec-butyl-2,6-di-<br>tert-butylphenol .....                    | 34 |
| Reverse Mutation Test of 4-sec-butyl-2,6-di-tert-butylphenol on Bacteria. ....   | 35 |
| Twenty-eight-day Repeated Dose Oral Toxicity Test of 4-sec-Butyl-2,6-di-<br>tert-butylphenol in Rats .....             | 36 |
| Legal Entities .....   | 37 |
| National Institute of Health Sciences, Japan .....   | 37 |

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# DOSSIER:

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**UUID:** 0

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**Author:**

**Date:** 2022-12-16T14:48:49.288+09:00

**Remarks:**

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## Dossier header

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## Dossier submission type

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**Name**

Complete table of contents

**Version**

core 7.0

**Name (given by user)**

## Dossier subject

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**Dossier subject**

[4-sec-Butyl-2,6-di-tert-butylphenol / 4-sec-butyl-2,6-di-tert-butylphenol / 17540-75-9](#)

**Public name**

4-sec-Butyl-2,6-di-tert-butylphenol

**Submitting legal entity**

[National Institute of Health Science](#)

**Dossier creation date/time**

Fri, 16 Dec 2022, 14:48:49+0900

**Used in category**

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# LEGAL\_ENTITY: National Institute of Health Science

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**UUID:** f51e7b54-9211-4863-90ce-fcf8a155d647

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**Remarks:**

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## General information

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**Legal entity name**

National Institute of Health Science

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# 4-sec-Butyl-2,6-di-tert-butylphenol

## CORE

### General information

#### Assessment approach (assessment entities)

FIXED\_RECORD: Assessment approach

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**UUID:** a253430f-9d8b-3bf9-87dd-d3aa6c1c3e03

**Dossier UUID:**

**Author:**

**Date:** 2020-03-24T16:11:36.000+09:00

**Remarks:**

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# OECD

## Health Effects

**Repeated dose toxicity:** oral

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

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**UUID:** e671a33a-d6fc-4e25-a27f-e5c467cea51f

**Dossier UUID:**

**Author:**

**Date:** 2022-12-16T14:46:37.761+09:00

**Remarks:**

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## Administrative data

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**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

## Data source

---

**Reference**

[Twenty-eight-day Repeated Dose Oral Toxicity Test of 4-sec-Butyl-2,6-di-tert-butylphenol in Rats / 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

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**Guideline**

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

**Deviations**

no

**GLP compliance**

yes

**Limit test**

no

---

**Test material****Test material information**

[4-sec-butyl-2,6-di-tert-butylphenol](#)

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

- Analytical purity: 99.0%
- Storage condition of test material: Stored in a refrigerator (2 - 9°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: CrI:CD(SD)

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

- Source: Charles River Japan, Inc., Atsugi Breeding Center.
- Age at study initiation: 5 weeks old
- Weight at study initiation: male 175.0 g (163-185 g), female 147.7 g (131-162 g)
- Housing: Animals were individually housed in bracket-type metallic wire-mesh cages (260W × 380D × 170H mm)
- Diet: Solid feed (CRF-1: Oriental Yeast Co., Ltd.) was given ad libitum.
- Water: Tap water was given ad libitum.
- Acclimation and quarantine period: male 5 days, female 6 days

**ENVIRONMENTAL CONDITIONS**

- Temperature (°C): 22±3 (actual temperature: 21-24°C)
- Humidity (%): 50±20% (actual humidity: 38-54%)
- Air changes (per hr): 10-15
- Photoperiod (hrs dark / hrs light): 12 hr dark/12 hr light (light: 8:00~20:00)

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**Administration / exposure****Route of administration**

oral: gavage

**Vehicle**

corn oil

---

**Details on oral exposure**

- Amount of vehicle (if gavage): 10 mL/kg
- Dosing volume: 10 mL/kg

**Analytical verification of doses or concentrations**

yes

**Duration of treatment / exposure**

28 days

**Frequency of treatment**

once a day

**Doses / concentrations**

|                     |                                     |
|---------------------|-------------------------------------|
| <b>Dose / conc.</b> |                                     |
| 0                   | mg/kg bw/day (actual dose received) |
| <b>Dose / conc.</b> |                                     |
| 15                  | mg/kg bw/day (actual dose received) |
| <b>Dose / conc.</b> |                                     |
| 60                  | mg/kg bw/day (actual dose received) |
| <b>Dose / conc.</b> |                                     |
| 250                 | mg/kg bw/day (actual dose received) |

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

Control and high-dose group: 12 animals/sex/ (including recovery group of 6 animals/sex/each group)

Low- and middle-dose group: 6 animals/sex/dose

**Control animals**

yes, concurrent vehicle

**Details on study design**

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

[14-day preliminary study]

In a dose finding study for a 28 day study, Crl:CD(SD) rats were given 4-sec-Butyl-2,6-di-tert-butylphenol at 0 (corn oil), 15, 60, 250 or 1000 mg/kg bw/day for 14 days. At 250 mg/kg bw/day and higher, increase in the liver weights were observed. At 1000 mg/kg bw/day, tendency decreased body weight gain, tendency decreased food consumption, increase in total bilirubin and BUN, soft stool, dilatation of gastrointestinal tract, dark reddish change of cauda epididymis were observed.



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

## Examinations

---

### Observations and examinations performed and frequency

CLINICAL OBSERVATIONS: Yes

- Time schedule: every day during the administration (twice a day: am and pm) and recovery periods (twice a day: am and pm).

DETAILED CLINICAL OBSERVATIONS: Yes

- Time schedule: Once prior to dosing and once during each study week (administration days 7, 14, 21, 28 and recovery days 7, 14).

BODY WEIGHT: Yes

- Time schedule for examinations: Before administration (on days 1, 4, 7, 14, 21 and 28 of the administration period, days 7 and 14 of the recovery period) and the necropsy days after completion of every period.

FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study):

- Food consumption: Yes. Before administration (on days 1, 4, 7, 14, 21 and 28 of the administration period and days 7 and 14 of the recovery period)

OPHTHALMOSCOPIC EXAMINATION: No

HAEMATOLOGY: Yes

- Time schedule for collection of blood: the after completion of the administration and recovery periods
- Anaesthetic used for blood collection: ether
- Animals fasted: Yes (16-19 hours)
- How many animals: all animals
- Parameters examined included RBC, hemoglobin, hematocrit, MCV, MCH, MCHC, platelet, reticulocyte, PT, APTT, WBC and differential WBC.

CLINICAL CHEMISTRY: Yes

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

URINALYSIS: Yes

- Time schedule for collection of urine: on weeks 4 of the administration period and weeks 2 of the recovery period.
- Metabolism cages used for collection of urine: Yes
- Animals fasted: No
- How many animals: all animals
- Parameters examined included color, urine volume, specific gravity, pH, protein, glucose, ketone body, bilirubin, occult blood and urobilinogen.

NEUROBEHAVIOURAL EXAMINATION: Yes

- Time schedule for examinations: On week 4 of administration period and week 2 of recovery period.
- Dose groups that were examined: All animals
- Battery of functions tested:

- 
- 1) Sensory/Reflex test: Visual reactivity, touch reactivity, auditory reactivity, pain reactivity, proprioceptive reactivity and aerial righting reflex.
  - 2) Measurement of Grip Strength. Grip strength of forelimb and hind limb was measured by CPU gauge (Aikoh Engineering Co., Ltd.).
  - 3) Measurement of Motor Activity. Motor activity was measured by a motor activity sensor for experimental animals SUPERMEX & CompAct (Muromachi Kikai Co., Ltd.). The measurement was conducted for 1 hour, and measured values at 10-minute intervals and from 0 to 60 minutes was collected.

### **Sacrifice and pathology**

GROSS PATHOLOGY: Yes

ORGAN WEIGHT: Yes [brain, pituitary gland, thyroid, adrenal, spleen, heart, liver, kidney, thymus, testis, epididymis, prostate, seminal vesicles (including coagulation gland), ovary, uterus]

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

### **Statistics**

The homoscedasticity was analyzed by Bartlett's test for data of grip strength, motor activity, body weight, body weight gain, food consumption, urine volume, hematological test, biochemical test, organ weight and organ weight ratio. When homogeneity was recognized, one-way analysis of variance (homogeneous data) or Kruskal-Wallis (non-homogeneous data) was conducted. If a significant difference was detected, as the result of one-way analysis of variance, Dunnett's method was applied for comparisons between control and individual treatment groups. And in the case of a significant difference was detected on Kruskal-Wallis, Mann-Whitney's U-test was applied for the same purpose. The trend by the group was analyzed by Kruskal-Wallis for general appearance, detailed clinical observation, qualitative items of urinary findings, and urine specific gravity. If a significant difference was detected as the result of Kruskal-Wallis, Mann-Whitney's U-test as applied for comparisons between control and individual treatment groups.

## **Results and discussion**

---

### **Results of examinations**

---

#### **Clinical signs**

effects observed, treatment-related

#### **Mortality**

no mortality observed

#### **Body weight and weight changes**

no effects observed

#### **Food consumption and compound intake (if feeding study)**

no effects observed

#### **Food efficiency**

not examined

#### **Water consumption and compound intake (if drinking water study)**

not examined

#### **Ophthalmological findings**

not examined

---

**Haematological findings**

effects observed, treatment-related

**Clinical biochemistry findings**

effects observed, treatment-related

**Urinalysis findings**

effects observed, treatment-related

**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

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

[At the dosing period]

Soft feces was observed in both sexes receiving 250 mg/kg bw/day.

[At the recovery period]

There were no changes related to the test substance in any groups.

**BODY WEIGHT AND WEIGHT GAIN**

There were no changes related to the test substance in any groups during the dosing.

**FOOD CONSUMPTION**

There were no changes related to the test substance in any groups during the dosing.

**HAEMATOLOGY**

[At the end of the dosing period]

Prothrombin time was prolonged in males receiving 60 mg/kg bw/day and above. Increased activated partial thromboplastin time was observed in males receiving 60 mg/kg/day and above and females receiving 250 mg/kg bw/day.

[At the end of the recovery period]

There were no changes related to the test substance in any groups.

**CLINICAL CHEMISTRY**

[At the end of the dosing period]

An increase in total cholesterol was observed in females receiving 15 mg/kg bw/day and above and in males receiving 60 mg/kg bw/day and above. An increase in total bilirubin was observed in both sexes receiving 250 mg/kg bw/day, increases in AST, ALT, ALP and BUN, and decreases in K and IP were observed in males receiving 250 mg/kg bw/day, and increases in alfa1-globulin protein fraction% and creatinine were observed in females receiving 250 mg/kg bw/day.

[At the end of the recovery period]

There were no changes related to the test substance in any groups.

**URINALYSIS**

[At the dosing period]

A decrease in urine pH was observed in females receiving 250 mg/kg bw/day.

---

[At the recovery period]

There were no changes related to the test substance in any groups.

#### NEUROBEHAVIOUR

There were no changes related to the test substance in any groups during the dosing.

#### ORGAN WEIGHTS

[At the end of the dosing period]

An increase in relative liver weight was observed in females receiving 15 mg/kg bw/day and above, an increase in absolute liver weight was observed in females receiving 250 mg/kg bw/day.

[At the end of the recovery period]

An increase in relative liver weight was observed in females receiving 250 mg/kg bw/day.

#### GROSS PATHOLOGY

[At the end of the dosing period]

Cecum: Watery contents were observed in males receiving 60 mg/kg bw/day and above and in females receiving 250 mg/kg bw/day.

[At the end of the recovery period]

There were no changes related to the test substance in any groups.

#### HISTOPATHOLOGY: NON-NEOPLASTIC

[At the end of the dosing period]

Liver: Slightly centrilobular hypertrophy of hepatocytes were observed in females receiving 250 mg/kg bw/day.

[At the end of the recovery period]

There were no changes related to the test substance in any groups.

---

## Effect levels

**Key result**

true

**Dose descriptor**

NOAEL

**Effect level**

15

mg/kg bw/day (actual dose received)

**Based on**

test mat.

**Sex**

male

**Basis for effect level**

gross pathology

Watery contents of cecum were observed in males receiving 60 mg/kg bw/day and above.

---

## 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/PDF17540-75-9b.pdf](https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF17540-75-9b.pdf)

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## Applicant's summary and conclusion

---

### Conclusions

Based on the findings in haematological examination, clinical chemistry, organ weight, and gross pathology, the NOAEL for repeated-dose toxicity of 4-sec-butyl-2,6-di-tert-butylphenol was determined to be 15 mg/kg bw/day.

### Executive summary

The repeated-dose toxicity of 4-sec-butyl-2,6-di-tert-butylphenol was assessed with the use of rats. Male and female rats (6 animals/sex/dose) were administered with 0 [vehicle: corn oil], 15, 60, and 250 mg/kg bw/day of 4-sec-butyl-2,6-di-tert-butylphenol for 28 days. Six of the 12 animals/sex that have received 0 and 250 mg/kg bw/day were selected to be part of a 14-day recovery group.

No treatment-related deaths were noted for both sexes. Clinical signs have shown that the doses did not affect the manipulative test, body weight, and food consumption. In general appearance, the male and female groups receiving 250 mg/kg bw/day had soft feces. The urinalysis shows the urine pH in females receiving 250 mg/kg bw/day was significantly decreased. Hematological parameters, such as prothrombin time in males in the  $\geq 60$  mg/kg bw/day group as well as activated partial thromboplastin time in males in the  $\geq 60$  mg/kg bw/day group and in females in the 250 mg/kg bw/day group, were significantly prolonged. Blood chemistry analysis has shown that total cholesterol level in females receiving  $\geq 15$  mg/kg bw/day and in males receiving  $\geq 60$  mg/kg bw/day and total bilirubin level in both sexes receiving 250 mg/kg bw/day significantly increased. Contrarily, the levels of potassium (K) and inorganic phosphorus (IP) significantly decreased in male rats receiving 250 mg/kg bw/day. A gross pathological examination has shown watery content of cecum in males receiving 60 mg/kg bw/day and in both sexes receiving 250 mg/kg bw/day. Soft feces, watery content of cecum, and decreases of K and IP levels were discovered, suggesting that the digestive tract is affected. There has been significantly increase in the relative weight of the liver of females receiving  $\geq 15$  mg/kg bw/day and the absolute weight of the liver of females receiving 250 mg/kg bw/day. Histopathological findings declared a slight hypertrophy of centrilobular hepatocytes in females receiving 250 mg/kg bw/day. These changes were no longer observed after the recovery period, showing that they were reversible. Founded on these effects of the cecum at 60 mg/kg bw/day in males, the no-observed-adverse-effect level (NOAEL) for repeated-dose toxicity of 4-sec-butyl-2,6-di-tert-butylphenol was 15 mg/kg bw/day in rats.

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## Genetic toxicity in vitro

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

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**UUID:** 0446cc20-0c98-4c91-8609-5eee0e1f8326

**Dossier UUID:**

**Author:**

**Date:** 2020-03-26T15:44:02.000+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

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 4-sec-butyl-2,6-di-tert-butylphenol on Bacteria. / MHLW, Japan / study report](#)

### Data access

data published

## Materials and methods

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### Test guideline

#### Qualifier

according to guideline

#### Guideline

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

---

**Deviations**

no

**Qualifier**

according to guideline

**Guideline**

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

**Deviations**

no

**GLP compliance**

yes

**Type of assay**

bacterial reverse mutation assay  
in vitro gene mutation study in bacteria

## Test material

**Test material information**

[4-sec-butyl-2,6-di-tert-butylphenol](#)

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

Purity 99.0%

## 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, TA1537 strains)

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

+S9 mix:

156, 313, 625, 1250, 2500, 5000 µg/plate (TA100, TA1535, TA98, TA1537 strains)

156, 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, no growth inhibition was observed at any dose.

---

**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:

**Remarks**

-S9 mix: 2-(2-Furyl)-3-(5-nitro-2-furyl) acrylamide (TA 100, TA98 and WP2 uvrA/pKM101), sodium azide (TA1535) and 9-aminoacridine hydrochloride monohydrate (TA1537). +S9 mix: 2-aminoanthracene (TA100, TA1535, WP2 uvrA/pKM101, TA98 and TA1537)

**Details on test system and experimental conditions**

METHOD OF APPLICATION: Preincubation

DURATION- Preincubation period: 20 min at 37°C

- Exposure duration: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**

other: S. typhimurium TA 1535, TA 1537, TA 98 and TA 100 bacterias

**Metabolic activation**

with and without

**Genotoxicity**

negative



---

**Cytotoxicity / choice of top concentrations**

no cytotoxicity

**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**

no cytotoxicity

**Vehicle controls validity**

valid

**Untreated negative controls validity**

not examined

**Positive controls validity**

valid

**Remarks on result**

other: all strains/cell types tested Migrated from field 'Test system'.

**Any other information on results incl. tables** 

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

[https://dra4.nihs.go.jp/mhlw\\_data/home/pdf/PDF17540-75-9e.pdf](https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF17540-75-9e.pdf)

*Please also see the attached files (Tables in English)*

**Applicant's summary and conclusion** 

---

**Conclusions**

Interpretation of results (migrated information): negative

In a bacterial reverse mutation assay using *Salmonella typhimurium* TA100, TA1535, TA98, and TA 1537, and *Escherichia coli* WP2uvrA/pKM101 (OECD TG 471), 4-sec-butyl-2,6-di-tert-butylphenol was negative with or without metabolic activation.

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

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**Dossier UUID:**

**Author:**

**Date:** 2020-03-17T14:56:12.000+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

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 4-sec-butyl-2,6-di-tert-butylphenol on Cultured Chinese Hams / MHLW, Japan / study report](#)

### Data access

data published

## Materials and methods

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### Test guideline

#### Qualifier

according to guideline

#### Guideline

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

#### Deviations

no

---

**Qualifier**

according to guideline

**Guideline**

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

**Deviations**

no

**GLP compliance**

yes

**Type of assay**

other: in vitro mammalian chromosome aberration test

---

**Test material****Test material information**

4-sec-butyl-2,6-di-tert-butylphenol

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

Purity 99.0%

---

**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): 10.2, 20.5, 40.9, 81.9, 164, 328, 655, 1310, 2620 ug/mL (IC50=15.1 ug/mL)

+S9 mix (short-term treatment): 10.2, 20.5, 40.9, 81.9, 164, 328, 655, 1310, 2620 ug/mL (IC50=29.0 ug/mL)

-S9 mix (continuous treatment, 24hr): 10.2, 20.5, 40.9, 81.9, 164, 328, 655, 1310, 2620 ug/mL (IC50=14.4 ug/mL)

Main study

-S9 (short-term treatment): 2.5, 5, 10, 13.3, 16.7 20 ug/mL

+S9 (short-term treatment): 5, 10, 20, 26.7, 33.3 ug/mL

+S9 (short-term treatment) (confirmatory test): 10, 20, 26.7, 33.3, 40 ug/mL

-S9 (continuous treatment, 24hr): 2.5, 5, 10, 13.3, 16.7, 20 ug/mL

-S9 (continuous treatment, 24hr) (confirmatory test): 4, 6, 8, 10, 11, 12, 13, 14, 15 ug/mL

**Vehicle / solvent**

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

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## 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]: benzo(a)pyrene

## Details on test system and experimental conditions

METHOD OF APPLICATION: Exposure duration: [short-term treatment]: 6 hrs + 18 hr, [continuous treatment]: 24 hr

SPINDLE INHIBITOR: Colcemid

STAIN: Giemsa stain (2 v/v%) for 20 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(±): 5% or more and less than 10%, Positive(+): 10% or more

## Statistics

no

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# Results and discussion

## Test results

### Key result

true

### Species / strain

other: Chinese hamster lung (CHL/IU) cells

### Metabolic activation

without

### Genotoxicity

negative

### Cytotoxicity / choice of top concentrations

cytotoxicity

### Vehicle controls validity

valid

### Untreated negative controls validity

not examined

---

**Positive controls validity**

valid

**Key result**

true

**Species / strain**

other: Chinese hamster lung (CHL/IU) cells

**Metabolic activation**

with

**Genotoxicity**

other: equivocal

**Cytotoxicity / choice of top concentrations**

cytotoxicity

**Vehicle controls validity**

valid

**Untreated negative controls validity**

not examined

**Positive controls validity**

valid

**Additional information on results**

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

[https://dra4.nihs.go.jp/mhlw\\_data/home/pdf/PDF17540-75-9f.pdf](https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF17540-75-9f.pdf)

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**Applicant's summary and conclusion****Conclusions**

Interpretation of results (migrated information):

equivocal with metabolic activation

negative without metabolic activation

The in vitro chromosomal aberration test using CHL/IU cells (OECD TG 473) was equivocal with metabolic activation.

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## Toxicity to reproduction

ENDPOINT\_STUDY\_RECORD: Toxicity to reproduction.001

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UUID: f2efea51-6b6b-4539-a905-c1f8ce22b37a

Dossier UUID:

Author:

Date: 2022-12-16T14:48:14.279+09:00

Remarks:

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## Administrative data

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### Endpoint

screening for reproductive / developmental toxicity

### 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

[Reproduction/Developmental Toxicity Screening Test on 4-sec-butyl-2,6-di-tert-butylphenol / MHLW, Japan / study report](#)

### Data access

data published

## Materials and methods

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### Test guideline

#### Qualifier

according to guideline

#### Guideline

OECD Guideline 421 (Reproduction / Developmental Toxicity Screening Test)

### GLP compliance

yes

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## Test material

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### Test material information

4-sec-butyl-2,6-di-tert-butylphenol

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

- Analytical purity: 99.0%
- Storage condition of test material: Stored in a refrigerator (3 - 9°C)
- Stability under test conditions: The stability of test material was identified by analysis of the remainder.

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## Test animals

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### Species

rat

### Strain

other: CrI:CD(SD)

### Sex

male/female

### Details on test animals or test system and environmental conditions

Sixty two male and 62 female Note) Sprague-Dawley strain SPF rats [CrI:CD(SD), Atsugi Breeding Center, Charles River Laboratories Japan, Inc.] were purchased at 8 weeks of age and quarantined/acclimated for 18 days counting the day of receipt as day 1 of acclimation and including the quarantine period of 3 days.

The body weight range at the start of administration was 405 to 494 g (mean body weight: 451 g) for males and 227 to 272 g (mean body weight: 244 g) for females.

Animals were housed individually and subsequently in male-female pairs during the mating period in bracket-type metallic wire-mesh cages (W 254 × D 350 × H 170 mm: Lead Engineering Co., Ltd.) in an animal room (Room No. 905) where the temperature was maintained at  $23 \pm 3^{\circ}\text{C}$  (measured values: 21-25°C), the relative humidity at  $50 \pm 20\%$  (measured values: 42-65%), the air ventilation at 10 to 15 times per hour and 12-hour lighting per day (07:00 to 19:00). From day 17 of gestation to day 4 of lactation, animals were housed in the unit of litter in plastic Econ cages (W 340 × D 400 × H 185 mm: CLEA Japan, Inc.) with bedding (Whiteflakes: Charles River Laboratories Japan, Inc.).

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## Administration / exposure

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### Route of administration

oral: gavage

### Vehicle

corn oil

### Details on exposure

Corn oil was selected as the vehicle since the stability of the test article in corn oil was favorable in the study for validation of the analytical method for determination of the test article concentration in test solutions and stability (Study No. A-2262) which was conducted before this study.

### Details on mating procedure

Males and females in the same dose group of the main groups were co-housed overnight on a one-to-one basis after the end of the pre-mating administration period. Copulation was considered successful if the formation of vaginal plugs or presence of sperm in vaginal smears was confirmed the following morning. The length of the mating period for the same male and female was 14 days at maximum.

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Delivery and delivery/lactation status: All copulated females were allowed to deliver spontaneously and examined for any abnormality of delivery. Dams which completed delivery were observed for clearance of placenta and amnion, and the end of delivery was designated as day 0 of lactation. Dams were then allowed to nurse their liveborn pups until day 4 of lactation and examined for lactation status using the gathering of pups, nesting and lactating as indicators.

**Analytical verification of doses or concentrations**

yes

**Details on analytical verification of doses or concentrations**

For the test solutions at all dose concentrations to be used for administration in week 1 or week 6 of administration, dose concentrations were verified by the HPLC method at Gotemba Laboratory, Bozo Research Center Inc. before use for administration. In the results, the percentage of the test article concentration in each dose concentration to the nominal concentration was in the range from 94.2 to 102.1%, which was within the acceptable range (concentration: within  $100.0 \pm 10.0\%$  of the nominal value)

**Duration of treatment / exposure**

Males: 42 days Females: 42-46 days from 14 days before mating to day 4 of lactation

**Frequency of treatment**

Once a day

**Doses / concentrations**

|                     |              |
|---------------------|--------------|
| <b>Dose / conc.</b> |              |
| 0                   | mg/kg bw/day |
| <b>Dose / conc.</b> |              |
| 12                  | mg/kg bw/day |
| <b>Dose / conc.</b> |              |
| 60                  | mg/kg bw/day |
| <b>Dose / conc.</b> |              |
| 300                 | mg/kg bw/day |

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

The number of animals per group was 12 animals of each sex

**Control animals**

yes, concurrent vehicle

**Details on study design**

The dose levels of this study were selected based on the results of the previously conducted study (dose-finding study). In the dose-finding study, death occurred at 1000 mg/kg and effects on general



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condition, hematology and blood chemistry examinations at 300 mg/kg and a high value in liver weight at 100 mg/kg and above. At 100 and 300 mg/kg, there were no clear effects from administration of the test article on body weight or food consumption. In the dose-finding study, there were mortalities in 1000 mg/kg group. In the 300 mg/kg group, some changes were observed in clinical observation, hematological examination and blood chemistry examination, and organ weight of the liver showed high value in the 100 mg/kg group and above. In the 100 and 300 mg/kg groups, there were no changes which were thought to be effects from administration of the test article in body weight or food consumption. Based on these results, the high dose in this reproduction/developmental toxicity screening test was set at 300 mg/kg, and the lower doses were set at 60 and 12 mg/kg using the common ratio of approximately 5.

#### **Positive control**

no

## **Examinations**

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#### **Parental animals: Observations and examinations**

Clinical observation performed and frequency: General condition was observed 3 times a day during the administration period (before dosing, and immediately after and approximately 2 hours after dosing).

Body weights were determined on days 1 (before dosing), 4, 8, 11, 15, 18, 22, 25, 29, 32, 36, 39, 42 of administration for males and on days 1, 4, 8, 11, 15 of administration, days 0, 4, 7, 11, 14, 17 and 20 of gestation, days 0 and 4 of lactation for females and the day of necropsy in males and females.

Food consumption was determined on days 1, 4, 8, 11, 15, 32, 36, 39 and 42 of administration for males and on days 1, 4, 8, 11 and 15 of administration and on days 1, 4, 7, 11, 14, 17 and 20 of gestation and days 2 and 4 of lactation in females, but it was not determined during the mating period for males and females.

#### **Oestrous cyclicity (parental animals)**

Vaginal smear pictures were classified as proestrus, estrus, metestrus and diestrus and examined for the frequency of estrus and interval between estruses (estrous cycle).

#### **Postmortem examinations (parental animals)**

Dams which delivered pups were exsanguinated on day 5 of lactation. The numbers of corpora lutea and implantation sites were counted.

Necropsy: Detailed macroscopic examination was conducted on the organs/tissues throughout the body of each animal, including the external appearance, head, thorax and abdomen.

Measurement of organ weights: The testis and epididymis were determined.

Histopathological examination: The testis, epididymis, prostate and seminal vesicle in males at 0 and 300 mg/kg groups, the ovary, uterus and vagina in females at 0 and 300 mg/kg groups. In addition, all subject organs/tissues of dead animals, all the animals that had not delivered by day 25 of gestation, dams with total litter loss during the lactation period and all gross pathological lesions of all animals were examined.

#### **Postmortem examinations (offspring)**

Examination of liveborn pups: The numbers of liveborn pups and stillborn pups were counted on the day of birth. After liveborn pups were examined for any external abnormality, sexed and weighed, dams were allowed to nurse their pups. Liveborn pups were observed for mortality once daily until day 4 after birth. All liveborn pups were exsanguinated after measurement of body weight on day 4 after birth, necropsied and examined for any abnormality in organs/tissues, including those in the head, thorax and abdomen. Individual body weights of liveborn pups were recorded, and the average body weight per litter was calculated by sex.

Pathological examination were performed.

#### **Statistics**

Dunnnett's test for continuous data and Dunnnett-type mean rank test for quantal data were used.

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### **Reproductive indices**

no. of copulated animals, no. of males impregnated females, no. of pregnant females, no. of females that delivered liveborn pups, estrous cycle, gestational length, no. of corpora lutea, no. of implantation sites, total no. of liveborn and stillborn pups, no. of liveborn pups, sex ratio on day 0 and day 4 after birth, copulation index (no. of copulated animals / no. of animals housed together x 100), insemination index (no. of males that impregnated females / no. of copulated males x 100), fertility index (no. of pregnant females / no. of copulated females x 100)

### **Offspring viability indices**

delivery index (no. of females delivered liveborn pups / no. of pregnant females x 100), implantation index (no. of implantation sites / no. of corpora lutea x 100), stillbirth index (no. of stillborn pups / total no. of liveborn and stillborn pups x 100), index of external abnormalities (no. of pups with external abnormalities / no. of liveborn pups x 100), live birth index (no. of liveborn pups / no. of implantation sites x 100), and viability index on day 4 after birth (no. of surviving pups on day 4 after birth / no. of liveborn pups x 100)

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## **Results and discussion**

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

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

##### **Clinical signs**

effects observed, treatment-related

##### **Description (incidence and severity)**

In males in the 300 mg/kg group, soft feces were observed in 5-8 animals sporadically from week 4 of administration onward, and fracture of incisors in 1 animal in week 6 of administration. In females of the 300 mg/kg group, there were no abnormalities in clinical signs during the pre-mating administration period, but soft feces were observed sporadically in 1-3 animals from day 9 of gestation onward and one female each died on day 22 and day 23 of gestation showing hypothermia and/or emaciation. One female showed pale skin on day 1 of lactation and soft feces and emaciation on day 2 of lactation and another female showed soft feces on day 0 of lactation, hypothermia and emaciation on day 1 of lactation and pale skin and hemorrhage from the vaginal opening on day 2 of lactation and all pups of these two females died by day 2 of lactation.

##### **Mortality**

mortality observed, treatment-related

##### **Description (incidence)**

In the 300 mg/kg group, 1 female died on day 22 and day 23 of gestation.

##### **Body weight and weight changes**

effects observed, treatment-related

##### **Description (incidence and severity)**

In males in the 300 mg/kg group, body weight was lower than that of the control group from day 8 of administration, and the body weight on days 36, 39 and 42 of administration was significantly lower than that of the control group and body weight gain during the administration period was significantly lower than that of the control group.

##### **Food consumption and compound intake (if feeding study)**

effects observed, treatment-related

##### **Description (incidence and severity)**

Females in the 300 mg/kg group showed a significantly low value compared to that of the control group on day 8 of administration, a significantly high value on day 4 and a significantly low value on day

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ay 20 of gestation, but there were no significant differences in food consumption between the control group and this group during the lactation period.

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

effects observed, treatment-related

##### **Description (incidence and severity)**

Males showed low body weight on the day of necropsy and males and females showed a high value in the weight of the liver in the 300 mg/kg group, and males showed a high value in the weight of the liver in the 60 mg/kg group.

#### **Gross pathological findings**

effects observed, treatment-related

##### **Description (incidence and severity)**

In the females in the 300 mg/kg group that died, a female showed undernourishment, dilatation of the cecum, enlargement of the liver and small thymus, but the other female showed no macroscopic abnormalities. Both females had implantations. For the dams that had total litter loss in the 300 mg/kg group, undernourishment, pale skin, dilatation of the cecum, dark coloration of the kidney, small thymus, dark red focus in the eye, dark coloration of Harderian gland, dark coloration of the lung, small sublingual gland and submandibular gland, dark red focus in the forestomach and small spleen were observed. In males that were necropsied on schedule, dilatation of the cecum was observed in the 300 mg/kg group. In females that were necropsied on schedule, enlargement of the liver was observed in the 300 mg/kg group.

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

effects observed, treatment-related

##### **Description (incidence and severity)**

Dead animals showed mild hypertrophy of centrilobular hepatocytes and minimal vacuolation of centrilobular hepatocytes in the liver, minimal hypertrophy of bile duct epithelial cells and severe atrophy of the thymus. Among the dams that had total litter loss, the dams in the 300 mg/kg group showed hypertrophy of bile epithelium, vacuolation of centrilobular hepatocytes and necrosis of centrilobular hepatocytes in the liver, acute tubular necrosis, interstitial inflammatory cell infiltration and glomerular thrombus in the kidney, atrophy of the thymus, diffuse mucosal hyperplasia of the cecum, ulcer and hyperplasia of squamous epithelium in the forestomach, increased porphyrin in Harderian gland, atrophy of submandibular gland, atrophy of the spleen, cell infiltration and thrombus in the lung, and focal retinal hemorrhage in the eye. In the animals that were sacrificed on schedule, males and females showed hypertrophy of centrilobular hepatocytes in the liver in the 60 and 300 mg/kg groups and bile duct epithelial cell hypertrophy in the liver in the 300 mg/kg group. Otherwise the animal in the 300 mg/kg group showed single cell necrosis and diffuse hyperplasia in cecum mucosa.

## **Reproductive function / performance (P0)**

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#### **Reproductive function: oestrous cycle**

no effects observed

#### **Reproductive performance**

no effects observed

## **Effect levels (P0)**

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#### **Key result**

false

#### **Dose descriptor**

NOAEL

**Effect level**

12

mg/kg bw/day (nominal)

**Based on**  
test mat.**Sex**  
male**Basis for effect level**

organ weights and organ / body weight ratios  
increased liver weight  
histopathology: non-neoplastic  
hypertrophy of centrilobular hepatocytes in the liver

**Key result**  
true**Dose descriptor**  
NOAEL**Effect level**

60

mg/kg bw/day (nominal)

**Based on**  
test mat.**Sex**  
female**Basis for effect level**

reproductive performance  
A tendency of lowering in the delivery index, the number of liveborn, and live birth index and the tendency of high stillborn rate were observed in 300 mg/kg bw/day group. The tendency of low viability index on postnatal day 4 was seen in the 300 mg/kg bw/day group.

**Key result**  
false**Dose descriptor**  
NOAEL**Effect level**

300

mg/kg bw/day

**Based on**  
test mat.**Sex**  
male**Basis for effect level**

reproductive performance  
no effects

**Results: F1 generation**

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## General toxicity (F1)

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### Mortality / viability

no mortality observed

### Body weight and weight changes

no effects observed

### Gross pathological findings

no effects observed

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## Effect levels (F1)

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### Key result

false

### Dose descriptor

NOAEL

### Generation

F1

### Effect level

300

mg/kg bw/day

### Based on

test mat.

### Sex

male/female

### Basis for effect level

other: no effects on development

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## 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. [https://dra4.nihs.go.jp/mhlw\\_data/home/pdf/PDF17540-75-9c.pdf](https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF17540-75-9c.pdf)

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## Applicant's summary and conclusion

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### Conclusions

There was no effect of the test substance in the parental males and pup at 300 mg/kg bw/day, the NOAEL of paternal and developmental toxicities was 300 mg/kg bw/day group. On the other hand, as seen on the effects on general condition of dams and delivery at 300 mg/kg bw/day, the NOAEL of the maternal toxicity was 60 mg/kg bw/day. In conclusion, the overall NOAEL for the reproductive/developmental toxicity of 4-sec-butyl-2,6-di-tert-butylphenol in this study was 60 mg/kg bw/day.

### Executive summary

The reproduction/developmental toxicity screening test of 4-sec-butyl-2,6-di-tert-butylphenol was assessed in rats in accordance to the OECD test guideline (TG) 421. In this study, 4-sec-butyl-2,6-di-tert-butylphenol was administered via gavage at 0 [vehicle: corn oil], 12, 60 and 300 mg/kg bw/day.

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Males (12/dose) were then treated for 42 days, which include a 14-day premating period and subsequent mating period, while females (12/dose) were treated for 42–46 days, including 14-day premating, mating, and gestation periods until lactation day 4. There were no effects on fertility but a tendency of lowering in the delivery index, the number of liveborn, and live birth index and the tendency of high stillborn rate were observed in 300 mg/kg bw/day group. The tendency of low viability index on postnatal day 4 was seen in the 300 mg/kg bw/day group. Because there was no effect of the test substance in the parental males and pup at 300 mg/kg bw/day, the NOAEL of paternal and developmental toxicities was 300 mg/kg bw/day group. On the other hand, as seen on the effects on general condition of dams and delivery at 300 mg/kg bw/day, the NOAEL of the maternal toxicity was 60 mg/kg bw/day. In conclusion, the overall NOAEL for the reproductive/developmental toxicity of 4-sec-butyl-2,6-di-tert-butylphenol in this study was 60 mg/kg bw/day.

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## DOMAIN

### Substance

**SUBSTANCE:** 4-sec-Butyl-2,6-di-tert-butylphenol

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**UUID:** b2fce83d-cfa7-43d6-a1fc-c5819c7f46d7

**Dossier UUID:**

**Author:**

**Date:** 2022-12-16T14:48:26.652+09:00

**Remarks:**

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**Substance name**

4-sec-Butyl-2,6-di-tert-butylphenol

**Public name**

4-sec-Butyl-2,6-di-tert-butylphenol

**Legal entity**

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

**Contact persons**

## Identification of substance

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**Reference substance**

[4-sec-butyl-2,6-di-tert-butylphenol](#) / [4-sec-butyl-2,6-di-tert-butylphenol](#) / [17540-75-9](#) / [241-533-0](#)

**EC number**

241-533-0

**EC name**

EC Inventory

**CAS number**

17540-75-9

**CAS name**

**IUPAC name**

4-sec-butyl-2,6-di-tert-butylphenol

## Role in the supply chain

---

**Manufacturer**

false

**Importer**

false

**Only representative**

false

**Downstream user**

false

---

# References

## Reference Substances

### REFERENCE\_SUBSTANCE: 4-sec-butyl-2,6-di-tert-butylphenol

---

**UUID:** ECB5-4be93424-903c-4590-bb54-0a3185f73206

**Dossier UUID:**

**Author:**

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

**Remarks:**

---

**Reference substance name**

4-sec-butyl-2,6-di-tert-butylphenol

**IUPAC name**

4-sec-butyl-2,6-di-tert-butylphenol

## Inventory

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**Inventory number**

**Inventory name**

4-sec-butyl-2,6-di-tert-butylphenol

**Inventory**

EC Inventory

**Inventory number**

241-533-0

**CAS number**

17540-75-9

**Molecular formula**

C<sub>18</sub>H<sub>30</sub>O

**Description**

**CAS number**

17540-75-9

## Synonyms

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**Synonyms**

**Identity**

Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)-

**Identity**

Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)-



**Identity**

Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)-

**Molecular and structural information****Molecular formula**

C<sub>18</sub>H<sub>30</sub>O

**Molecular weight**

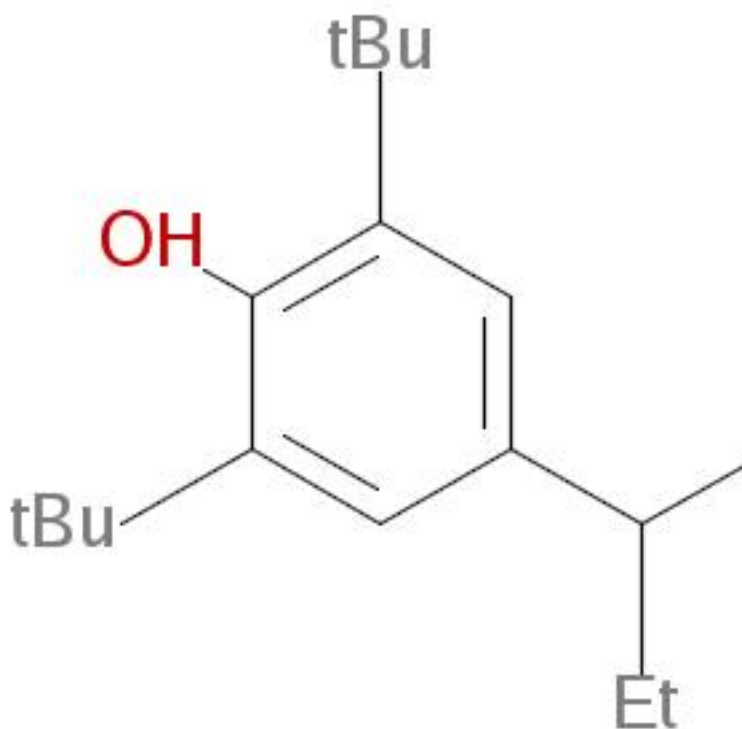
262.4302

**SMILES notation**

CCC(C)c1cc(c(O)c(c1)C(C)(C)C)C(C)(C)C

**InChI**

InChI=1/C<sub>18</sub>H<sub>30</sub>O/c1-9-12(2)13-10-14(17(3,4)5)16(19)15(11-13)18(6,7)8/h10-12,19H,9H2,1-8H3

**Structural formula****Related substances****Group / category information**

DSL Category: Organics

USEPA Category: Neutral Organics;Phenols

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## Test Materials

### TEST\_MATERIAL\_INFORMATION: 4-sec-butyl-2,6-di-tert-butylphenol

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**UUID:** 57eadf5d-9389-4ab3-ae7c-8517aed5eccc

**Dossier UUID:**

**Author:**

**Date:** 2019-12-17T14:59:36.000+09:00

**Remarks:**

---

**Name**

4-sec-butyl-2,6-di-tert-butylphenol

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## Literatures

### LITERATURE: In Vitro Chromosomal Aberration Test of 4-sec-butyl-2,6-di-tert-butylphenol on Cultured Chinese Hamster Cells.

---

**UUID:** 22775324-3017-4f58-8b64-05b57fe2b4ac

**Dossier UUID:**

**Author:**

**Date:** 2019-12-18T15:24:12.000+09:00

**Remarks:**

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## General information

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**Reference Type**

study report

**Title**

In Vitro Chromosomal Aberration Test of 4-sec-butyl-2,6-di-tert-butylphenol on Cultured Chinese Hamster Cells.

**Author**

MHLW, Japan

**Bibliographic source**

Japan Existing Chemical Data Base (JECDB) [https://dra4.nihs.go.jp/mhlw\\_data/home/pdf/PDF17540-75-9f.pdf](https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF17540-75-9f.pdf)

**Testing facility**

Safety Research Institute for Chemical Compounds Co., Ltd.

**Report number**

SR08225

---

# LITERATURE: Reproduction/Developmental Toxicity Screening Test on 4-sec-butyl-2,6-di-tert-butylphenol

---

**UUID:** 243fe436-3b37-405c-815a-22caee3481e2

**Dossier UUID:**

**Author:**

**Date:** 2020-02-18T11:14:20.000+09:00

**Remarks:**

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## General information

---

**Reference Type**

study report

**Title**

Reproduction/Developmental Toxicity Screening Test on 4-sec-butyl-2,6-di-tert-butylphenol

**Author**

MHLW, Japan

**Year**

2011

**Bibliographic source**

[https://dra4.nihs.go.jp/mhlw\\_data/home/pdf/PDF17540-75-9c.pdf](https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF17540-75-9c.pdf)

**Testing facility**

BoZo Research Center

---

## LITERATURE: Reverse Mutation Test of 4-sec-butyl-2,6-di-tert-butylphenol on Bacteria.

---

**UUID:** ae56849c-be2d-49f5-95a4-20dbe725402a

**Dossier UUID:**

**Author:**

**Date:** 2019-12-17T14:46:26.000+09:00

**Remarks:**

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### General information

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**Reference Type**

study report

**Title**

Reverse Mutation Test of 4-sec-butyl-2,6-di-tert-butylphenol on Bacteria.

**Author**

MHLW, Japan

**Bibliographic source**

Japan Existing Chemical Data Base (JECDB) [https://dra4.nihs.go.jp/mhlw\\_data/home/pdf/PDF17540-75-9e.pdf](https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF17540-75-9e.pdf)

**Testing facility**

Safety Research Institute for Chemical Compounds Co., Ltd.

**Report number**

SR08224

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# LITERATURE: Twenty-eight-day Repeated Dose Oral Toxicity Test of 4-sec-Butyl-2,6-di-tert-butylphenol in Rats

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## General information

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### Reference Type

study report

### Title

Twenty-eight-day Repeated Dose Oral Toxicity Test of 4-sec-Butyl-2,6-di-tert-butylphenol in Rats

### 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/PDF17540-75-9b.pdf](https://dra4.nihs.go.jp/mhlw_data/home/pdf/PDF17540-75-9b.pdf)

### Testing facility

Safety Research Institute for Chemical Compounds Co., Ltd.

### Report number

SR08226

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## Legal Entities

**LEGAL\_ENTITY: National Institute of Health Sciences,  
Japan**

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## General information

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