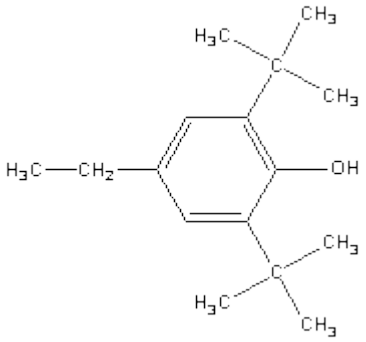
INITIAL TARGETED ASSESSMENT PROFILE

CAS No.	4130-42-1
Chemical Name	2,6-Di-*tert*-butyl-4-ethylphenol
Structural Formula	

SUMMARY CONCLUSIONS OF THE TARGETED ASSESSMENT

NOTE: The present assessment was targeted to address only the following endpoint(s): Human Health: repeated dose toxicity and *in vitro* mutagenicity. It cannot be considered as a full SIDS Initial Assessment. Summary information on exposure is also reported here. Other endpoints for human health and the environment have not been presented to OECD member countries, and thus are not included in this profile.

Rationale for targeting the assessment

Under the Japanese Chemical Substances Control Law, hazard assessment of existing chemical substances via environmental exposure has been conducted. If a chemical substance is evaluated as "not biodegradable (persistent)" and "not highly bioaccumulative", at least, a 28-day repeated dose toxicity and two *in vitro* mutagenicity studies are required as screening studies for hazard evaluation regarding human health. If a chemical is evaluated as having potential of long-term toxicity for human health, the chemical is classified as a Type II Monitoring Chemical Substance. If not, the chemical is of low priority for further action. Type II Monitoring Chemical Substances undergo risk-based management; at first, annual production volumes of those substances are monitored.

2,6-Di-*tert*-butyl-4-ethylphenol was evaluated as "not biodegradable (persistent)" and "low bioaccumulative" by METI (Ministry of Economy, Trade and Industry, Japan). Biodegradation and bioaccumulation are not part of the targeted assessment and therefore not presented in ITAP. In order to determine whether this chemical is classified as a Type II monitoring chemical substance, the initial hazard assessment of 2,6-di-*tert*-butyl-4-ethylphenol was conducted for the acute toxicity, repeated dose toxicity and mutagenicity by MHLW (Ministry of Health, Labour and Welfare, Japan) in December 2007.

This targeted assessment document was originally based on the material from the chemical assessment council of MHLW, and the toxicological profile was re-assessed for the OECD Cooperative Chemicals Assessment Programme.

Physical-Chemical Properties

2,6-Di-*tert*-butyl-4-ethylphenol is a yellow solid at room temperature. Melting point and boiling point are 44 °C and 272 °C respectively (both values are from CRC Handbook of Chemistry and Physics, version 2008). Measured partition coefficient between octanol and water (log Kow) is ≥ 3.27. Vapour pressure is calculated to

be 0.29 Pa at 25 °C. Measured water solubility is 21 mg/L at 25 °C.

Human Health

No information is available for the acute toxicity of 2,6-di-*tert*-butyl-4-ethylphenol. In a dose-finding study, rats were daily dosed by gavage with 2,6-di-*tert*-butyl-4-ethylphenol at 0, 125, 250, 500 or 1000 mg/kg bw/day for 14 days. Neither deaths nor clinical signs were observed on day 1 of administration. A total of 4/5 males and 3/5 females died on day 7-13 of administration at 1000 mg/kg bw/day.

A repeated dose oral toxicity study was conducted following a Guideline for 28-Day Repeated Dose Toxicity Test in Mammalian Species (Chemical Substances Control Law of Japan) under the principles of GLP. In this study, 2,6-di-*tert*-butyl-4-ethylphenol was administered to rats via gavage at 0 (vehicle control: 0.5% methylcellulose solution), 15, 60, or 250 mg/kg bw/day for 28 days. No deaths or clinical signs of toxicity were observed, and no significant changes were found in terms of body weight and urinalysis in any group. In the hematological and blood chemical examination, the changes were observed in only 250 mg/kg bw/day group. Platelet, fibrinogen and APTT were increased in both sexes, and PT was increased in only males. There was increased total cholesterol and total protein in both sexes, and increased phospholipid in females.

A decrease in Cl was noted in 250 mg/kg bw/day females. The absolute and relative weights of the liver were increased at 60 and 250 mg/kg bw/day in both sexes. Histopathological examination revealed centrilobular hypertrophy of hepatocytes in both sexes given 60 mg/kg bw/day and 250 mg/kg bw/day and hypertrophy of follicular cells in the thyroid in both sexes given 250 mg/kg bw/day and in males given 60 mg/kg bw/day. After the 14-day recovery period, histopathological changes and an increase in organ weight of the liver and thyroid were recovered, however increased platelet and serum total cholesterol remained. Based on the hypertrophy in the liver and thyroid and increased liver weight in both sexes at 60 mg/kg bw/day, the NOAEL of 2,6-di-*tert*-butyl-4-ethylphenol was concluded to be 15 mg/kg bw/day in rats.

In a bacterial mutation study using *Salmonella typhimurium* TA98, TA100, TA1535 and TA1537, and *Escherichia coli* WP2 *uvrA* [OECD TG 471], 2,6-di-*tert*-butyl-4-ethylphenol was negative with or without metabolic activation. In an *in vitro* chromosome aberration test using CHL/IU cells [OECD TG 473], 2,6-di-*tert*-butyl-4-ethylphenol was positive with metabolic activation. Based on these results, 2,6-di-*tert*-butyl-4-ethylphenol is considered to be genotoxic *in vitro*.

Agreed Hazard Conclusions

This chemical possesses properties indicating a hazard for human health endpoints (repeated dose toxicity and chromosomal aberrations *in vitro*) targeted in this assessment.

Available Exposure

Production and/or import volume of trialkyl (or alkenyl, C = 1 - 4) phenol, including 2,6-di-*tert*-butyl-4-ethylphenol, was reported to be 1,000 – 10,000 tonnes/year in the fiscal year 2007 in Japan (sponsor country). Specific Production and/or import volume of 2,6-di-*tert*-butyl-4-ethylphenol in the sponsor country is not available. Production and/or import volume of 2,6-di-*tert*-butyl-4-ethylphenol in the United States was 500,000 – 1,000,000 pounds (227 - 454 tonnes) according to 2006 Inventory Updated Reporting. Production volume in the world is not available.

2,6-Di-*tert*-butyl-4-ethylphenol is used as an antioxidant in the sponsor country. In 2006 Inventory Updated Reporting in the United States, it was reported that 2,6-di-*tert*-butyl-4-ethylphenol is used in rubber and plastic products.