SCREENING-LEVEL HAZARD CHARACTERIZATION
Alkylphenols Category

Sponsored Chemicals

o-Substituted Alkylphenols

***o-sec*-Butylphenol**	**CASRN 89-72-5**
***2-tert*-Butylphenol**	**CASRN 88-18-6**

p-Substituted Alkylphenols

***p-tert*-Butylphenol**	**CASRN 98-54-4**
***p-sec*-Butylphenol**	**CASRN 99-71-8**
***p-tert*-Amylphenol**	**CASRN 80-46-6**
Heptyl derivatives (*p*-heptylphenol)	**CASRN 72624-02-3**
***p-tert*-Octylphenol**	**CASRN 140-66-9**
***p*-Octylphenol**	**CASRN 1806-26-4**
***p*-(alpha, alpha-Dimethylbenzyl)phenol or *p*-cumylphenol**	**CASRN 599-64-4**
***p*-Nonylphenol**	**CASRN 84852-15-3**
***p*-Dodecylphenol**	**CASRN 210555-94-5**

Di- and Tri-Substituted Mixed Alkylphenols

2,4-Di-*tert*-Butylphenol	**CASRN 96-76-4**
2,6-Di- *tert*-Butylphenol	**CASRN 128-39-2**
2,4-Di-*tert*-pentylphenol	**CASRN 120-95-6**
2,4-Bis(alpha, alpha-dimethylbenzyl)phenol or *o,p*-cumylphenol or 2,4-di-cumylphenol	**CASRN 2772-45-4**
2,3,6-Trimethylphenol	**CASRN 2416-94-6**
4-sec-Butyl-2,6-tert-butylphenol	**CASRN 17540-75-9**
2,4,6-Tri-*tert*-butylphenol	**CASRN 732-26-3**

The High Production Volume (HPV) Challenge Program[1] was conceived as a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to "SIDS" (Screening Information Data Set[1,2])

[1] U.S. EPA. High Production Volume (HPV) Challenge Program; http://www.epa.gov/chemrtk/index.htm.
[2] U.S. EPA. HPV Challenge Program – Information Sources; http://www.epa.gov/chemrtk/pubs/general/guidocs.htm.

endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency's Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance[2,3] and is based primarily on hazard data provided by sponsors; however, in preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor's responses to comments and revisions made to the submission. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT's focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

These hazard characterizations are technical documents intended to inform subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and provide information previously not readily available to the public.

[3] U.S. EPA. Risk Assessment Guidelines; http://cfpub.epa.gov/ncea/raf/rafguid.cfm.

Chemical Abstract Service Registry Number (CASRN)	**Sponsored Chemical** ***o-Substituted Alkylphenols*** **CASRN 89-72-5** **CASRN 89-72-5** **CASRN 88-18-6** ***p-Substituted Alkylphenols*** **CASRN 98-54-4** **CASRN 99-71-8** **CASRN 80-46-6** **CASRN 72624-02-3** **CASRN 140-66-9** **CASRN 1806-26-4** **CASRN 599-64-4** **CASRN 84852-15-3** **CASRN 210555-94-5** ***Di- and Tri-Substituted Mixed Alkylphenols*** **CASRN 96-76-4** **CASRN 128-39-2** **CASRN 120-95-6** **CASRN 2772-45-4** **CASRN 2416-94-6** **CASRN 17540-75-9** **CASRN 732-26-3**
Chemical Abstract Index Name	***o-Substituted Alkylphenols*** **Phenol, 2-(1-methylpropyl)-2-*tert*-Butylphenol** **Phenol, 2-(1,1-dimethylethyl)-** ***p-Substituted Alkylphenols*** **Phenol, 4-(1,1-dimethylethyl)-** **Phenol, 4-(1-methylpropyl)-** **Phenol, 4-(1,1-dimethylpropyl)-** **Phenol, heptyl derivs.)** **Phenol, 4-(1,1,3,3-tetramethylbutyl)-**

	Phenol, 4-octyl-) **Phenol, 4-(1-methyl-1-phenylethyl)-** **Phenol, 4-nonyl-, branched)** **Phenol, 4-dodecyl-, branched)** ***Di- and Tri-Substituted Mixed Alkylphenols*** **Phenol, 2,4-bis(1,1-dimethylethyl)-** **Phenol, 2,6-bis(1,1-dimethylethyl)-** **Phenol, 2,4-bis(1,1-dimethylpropyl)-** **Phenol, 2,4-bis(1-methyl-1-phenylethyl)-** **Phenol, 2,3,6-trimethyl)-** **Phenol, 2,6-bis(1,1-dimethylethyl)-4-(1-methylpropyl)-** **Phenol, 2,4,6-tris(1,1-dimethylethyl)-**
Structural Formula	**See Section 1**

Summary

The members of the alkylphenols category contain both solid and liquid substances. Alkylphenols have low to moderate water solubility except for CASRN 2416-94-6 which has high water solubility. Vapor pressures range from low to moderate. They are expected to have low to moderate mobility in soil. Volatilization of the alkylphenols from water and moist soils is considered low to moderate based on their Henry's Law constants. The rate of hydrolysis is considered negligible for all members of the category. The rate of atmospheric photooxidation is considered moderate except for CASRN 2416-94-6 which is considered rapid. The alkylphenols are expected to have a range of persistence from moderate (P2) to high (P3) with persistence increasing with increasing degree of branching and bioaccumulation potential ranges from low (B1) to high (B3).

o-Substituted Alkylphenols

The acute toxicity is low by the oral route and moderate by the dermal route. Repeated-dose, reproductive, and developmental toxicity studies were not available for either member of the *o*-substituted alkylphenols subcategory (CASRNs 89-72-5 and 88-18-6). Members of this alkylphenols subcategory did not induce gene mutations in bacteria. Evaluation of chromosomal effects were not available for either member of this subcategory. Members of this subcategory are considered highly irritating or corrosive to the skin and irritating to eye.

For acute hazard of *o*-substituted alkylphenols subcategory, the estimated 96-hour LC_{50} to fish is 2.5 mg/L, the measured 48-hour EC_{50} to aquatic invertebrates is 1.3 mg/L, and the estimated 96-hour EC_{50} to aquatic plants is 5.8 mg/L .

Data gaps for repeated-dose/reproductive/developmental toxicity/and chromosomal effect studies for human health, and acute toxicity to fish and aquatic plants for environment were identified under the HPV Challenge Program for the *o*-substituted alkylphenols subcategory.

p-Substituted Alkylphenols

The acute toxicity is low by the oral and dermal routes. A combined repeated-dose/reproductive/developmental toxicity study by the oral route with CASRN 98-54-4 in rats showed a NOAEL for systemic toxicity of 200 mg/kg-bw/day (highest dose tested). In a 20-week repeated dose study with the same chemical in male hamsters, decreased body weight and liver weight, and forestomach hyperplasia were observed at the only dose tested (1800 mg/kg-bw/day). A repeated-dose toxicity study by the oral route in rats with CASRN 99-71-8 showed effects in the kidney, esophagus, and forestomach at a dose of 500 mg/kg-bw/day; the NOAEL was 150 mg/kg-bw/day. A repeated-dose toxicity study by the oral route in rats with CASRN 140-66-9 showed a NOAEL for systemic toxicity of 15 mg/kg-bw/day and a LOAEL of 150 mg/kg-bw/day (based on reductions in body weight gain). Two separate 28- and 90-day repeated-dose toxicity studies by the oral route in rats with CASRN 84852-15-3 showed decreases in body weight gain at 400 and 150 mg/kg-bw/day, respectively; the NOAEL for systemic toxicity was 100 and 50 mg/kg-bw/day, respectively. However, a multi-generation study (reported below) with the same chemical showed similar systemic toxic effects (decreases in body weight) at lower doses (43-64 mg/kg-bw/day) in adult animals. The combined repeated-dose/reproductive/developmental toxicity study with CASRN 98-54-4 by the oral route in rats showed no adult/reproductive/or developmental toxicity; the NOAEL for all effects was the highest tested dose of 200 mg/kg-bw/day. A two-generation reproductive toxicity study by the oral route in rats with CASRN 140-66-9 showed effects on body weights in adults at a dose of 100 mg/kg-bw/day; the NOAEL for adult systemic toxicity was 10 mg/kg-bw/day. There was no evidence of reproductive toxicity in this study and the NOAEL was 100 mg/kg-bw/day for males and 150 mg/kg-bw/day for females. In this same study, there was developmental toxicity at 150 mg/kg-bw/day as demonstrated by effects on pup body weights and delays in acquisition of vaginal opening and preputial separation; the NOAEL for developmental toxicity was 15 mg/kg-bw/day. A three-generation reproductive toxicity study by the oral route in rats with CASRN 84852-15-3 showed decreases in adult body weight at 43-64 mg/kg-bw/day; the NOAEL for systemic toxicity was 13-19 mg/kg-bw/day. This same study showed decreases in epididymal sperm density and testicular sperm head counts in males, and increased estrous cycle length and decreased ovarian weights in females at 43-64 mg/kg-bw/day; the NOAEL for reproductive toxicity was 13-19 mg/kg-bw/day. There was evidence of developmental toxicity in this study as demonstrated by acceleration in the vaginal opening in pups at 43-64 mg/kg-bw/day; the NOAEL for developmental toxicity was 13-19 mg/kg-bw/day. A prenatal developmental toxicity study in rats by the oral route with CASRN 84852-15-3 showed evidence of maternal toxicity as demonstrated by kidney and spleen effects in the dams at 150 mg/kg-bw/day; the NOAEL for maternal toxicity was 75 mg/kg-bw/day. There was no evidence of developmental toxicity in this study and the NOAEL was 300 mg/kg-bw/day. Members of this alkylphenols subcategory did not induce gene mutations in bacteria and did not induce chromosomal aberrations when tested *in vitro* or *in vivo*. Many members of this subcategory are considered highly irritating or corrosive to the skin and irritating to eye.

For acute hazard of *p*-substituted alkylphenols subcategory, the measured 96-hour LC_{50} values to fish range from 0.13 to 5.1 mg/L , the measured 48-hour EC_{50} values to aquatic invertebrates

range from 0.09 to 6.7 mg/L, and the measured 72/96-hour EC_{50} values to aquatic plants range from 0.06 to 22.7 mg/L . The measured chronic hazard of *p*-substituted alkylphenols subcategory ranges from 0.024 to 2.3 mg/L for 21-day *Daphnia magna* toxicity.

No data gaps were identified under the HPV Challenge Program for the *p*-substituted alkyphenols subcategory.

Di- and Tri-Substituted Alkylphenols

The acute toxicity is low by the oral route and moderate by the dermal route. A repeated-dose toxicity study by the oral route in rats with CASRN 128-39-2 showed increases in liver weight with corresponding histopathology at 600 mg/kg-bw/day; the NOAEL for systemic toxicity was 100 mg/kg-bw/day. A two-year repeated-dose toxicity study in rats by the oral route with CASRN 732-26-3 showed evidence of liver toxicity at 15 mg/kg-bw/day; the NOAEL for systemic toxicity was 5 mg/kg-bw/day. A combined reproductive and developmental toxicity screening study by the oral route in rats with limited postnatal evaluations with CASRN 128-39-2 showed marginal effects on body weights in adults and reduced viability and weight gain in the pups at 750 mg/kg-bw/day; the NOAEL for adult systemic and developmental toxicity was 150 mg/kg-bw/day. There was no evidence of reproductive toxicity in this study and the NOAEL was 750 mg/kg-bw/day. Members of this alkylphenols subcategory did not induce gene mutations in bacteria and did not induce chromosomal aberrations when tested *in vitro* or *in vivo*. Many members of this subcategory are considered moderately irritating to the skin. The two-year repeated-dose toxicity study in rats with CASRN 732-26-3 found no evidence of cancer.

For acute hazard of di- and tri-substituted alkylphenols subcategory, the measured/estimated 96-hour LC_{50} values to fish range from 0.02 to 14.8 mg/L , the measured/estimated 48-hour EC_{50} values to aquatic invertebrates range from 0.04 to 2.8 mg/L, and the measured/estimated 72/96-hour EC_{50} values to aquatic plants range from 0.1 to 19 mg/L . The estimated chronic hazard of *p*-substituted alkylphenols subcategory ranges from 0.008 to 0.08 mg/L for 21-day *Daphnia magna* toxicity.

A data gap for chronic toxicity to aquatic invertebrates was identified under the HPV Challenge Program for the di- and tri-substituted mixed alkylphenols subcategory.

The sponsor, Schenectady International, Inc. - Chemical Division (SII), submitted a Test Plan and Robust Summaries to EPA for the Alkylphenols Category on April 13, 2001. EPA posted the submission on the ChemRTK Web site on May 18, 2001 (http://www.epa.gov/chemrtk/pubs/summaries/alkylphn/c13007tc.htm). EPA comments on the original submissions were posted to the website on November 29, 2001. Public comments were also received and posted to the website. The sponsor submitted revised and final documents on April 1, 2002 and April 6, 2006, which were posted to the ChemRTK website on April 23, 2003 and June 9, 2006, respectively.

The original submission contained 1,1,3,3-tetramethylbutylphenol (CASRN 27193-28-8); however, the sponsor informed EPA that this chemical is no longer used and replaced it with *p-tert*-octylphenol (CASRN 140-66-9). In addition, SII has discontinued manufacturing of chemicals *p*-(alpha,alpha-dimethyl benzyl)phenol (CASRN 599-64-4) and *p*-octylphenol (CASRN 1806-26-4). However, the sponsor retained information on these chemicals in the test plan and it is considered in the hazard characterization. SII has also volunteered to sponsor *p-sec*-butylphenol (CASRN 99-71-8) and has revised the test plan and submitted robust summaries for this chemical.

Concerning the two category members identified as no longer being manufactured by SII, IUR information confirms that CASRN 1806-26-4 was not produced or imported into the US by any company; however, CASRN 599-66-4 was reported to be produced in the US by companies other than SII.

Category Justification

The 18 members of the alkylphenols category have a single common functional group, the phenolic hydroxyl. The category justification is based primarily on structural similarity of the chemicals and the expectation that the physicochemical and toxicological properties are similar as a result of their structures. In the submission, the sponsor grouped all chemicals into one category and proposed a read-across approach to extrapolate available data from the tested chemicals to the untested chemicals. EPA disagreed with this approach because it lacked the predictive strength to conduct the chemical-to-chemical extrapolations so broadly. For example, EPA did not agree that it was appropriate to assume that phenols with highly branched substituents in the 2-position (i.e., having a hindered phenolic group) would have toxicity similar to those without substituents at that position. EPA also considered the available mammalian data too limited to fully support general conclusions about alkylphenols as a class. For ecotoxicity, the category proposal did not take into account the wide range in lipophilicity across the undivided category. EPA therefore suggested that the sponsor consider smaller subcategories. In its revised submissions, the sponsor divided the category into three subcategories (ortho-substituted, para-substituted, and di-and tri- substituted alkylphenols) based on the position and the extent of substitution on the phenols. EPA agrees with this approach. Thus, read-across is reasonable and acceptable only within a subcategory.

1 Chemical Identity

1.1 Identification and Purity

The following description is taken from the 2002 Test Plan and Robust Summaries:

The members of the alkylphenols category differ according to the position(s) of the substituent, *ortho*, *meta*, *para*, or a combination of these; and type of substituent, either alkyl or benzyl. The side chains attached to the phenol ring tend to be highly branched. The manufacturing processes are conducted in fully automated, closed systems with a fixed bed reactor. The crude alkylphenol is rectified by fractional vacuum distillation to achieve a purity of test substance given as typically 98.5% minimum.

The chemical structures of the alkylphenols are depicted in Table 1.

Table 1: Alkylphenols Category Sponsored Chemical Structures

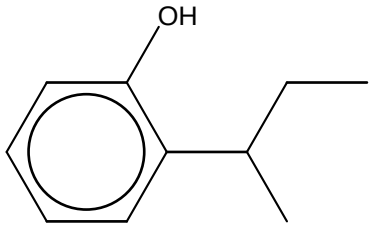
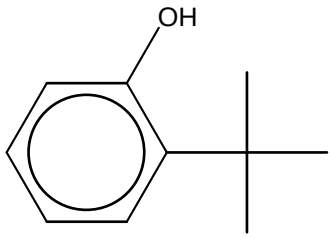
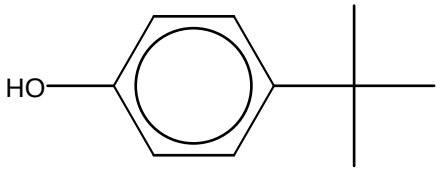
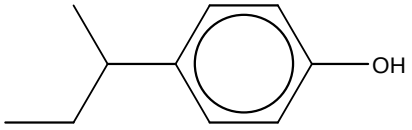
CASRN Name	CASRN	Chemical Structure
o-Substituted Alkylphenols		
o-sec-Butylphenol	89-72-5	
2-*tert*-Butylphenol	88-18-6	
p-Substituted Alkylphenols		
p-tert-Butylphenol	98-54-4	
p-sec-Butylphenol	99-71-8	

Table 1: Alkylphenols Category Sponsored Chemical Structures

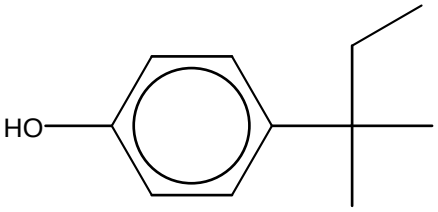
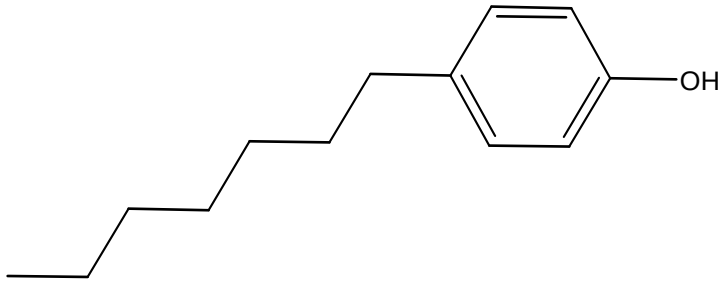
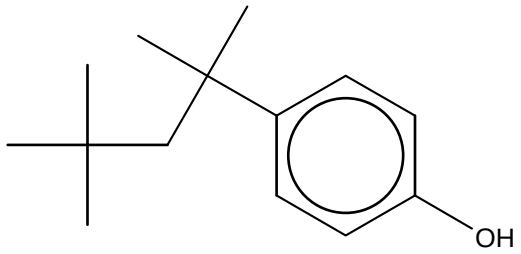
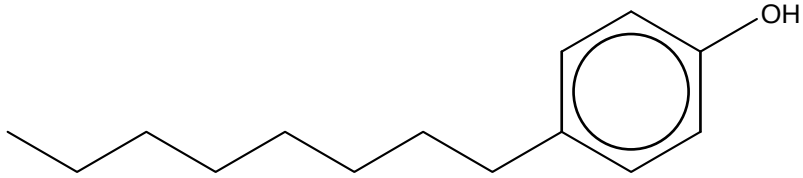
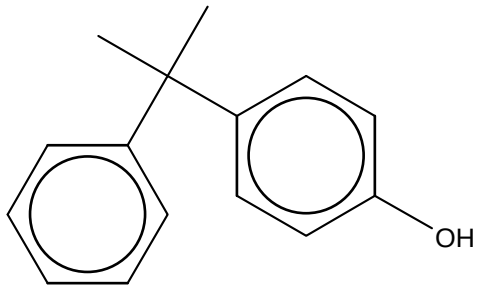
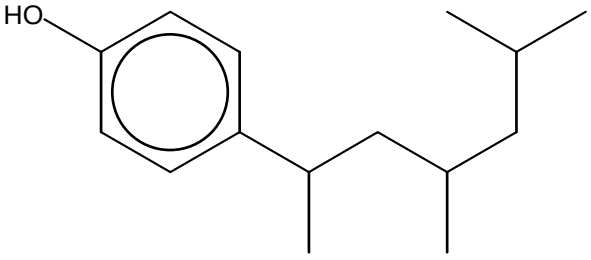
CASRN Name	CASRN	Chemical Structure
p-tert-Amylphenol	80-46-6	
Heptyl derivatives (*p*-heptylphenol)	72624-02-3	
p-tert-Octylphenol	140-66-9	
p-Octylphenol	1806-26-4	
p-(alpha, alpha Dimethylbenzyl)-phenol or *p*-cumylphenol	599-64-4	
p-Nonylphenol	84852-15-3	

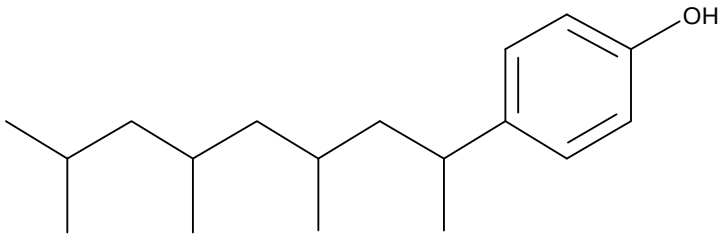
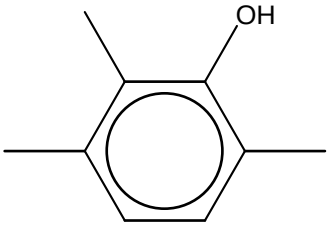
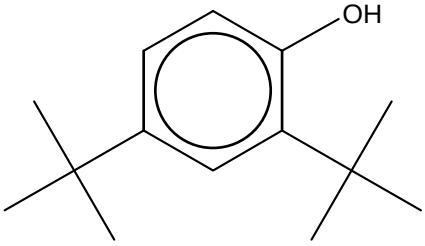
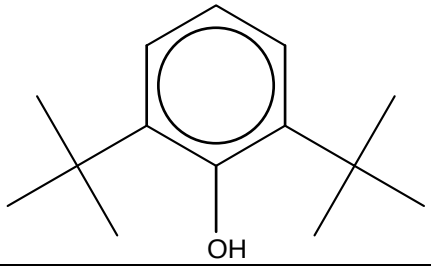
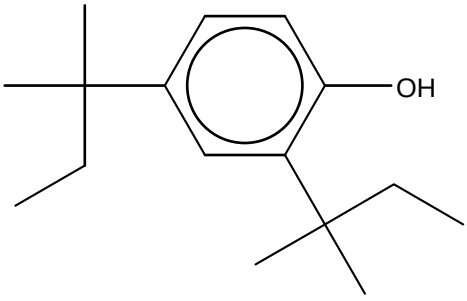
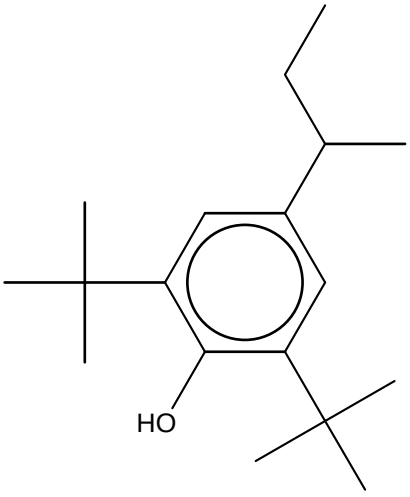
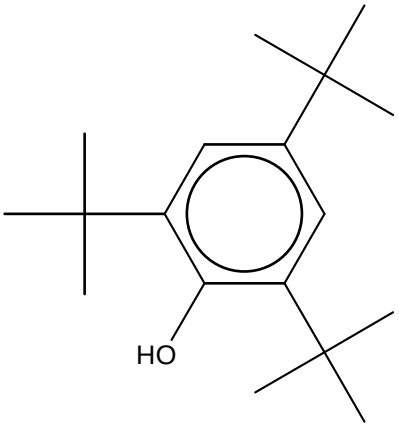
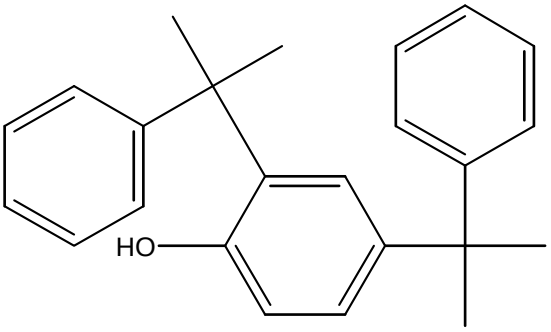
Table 1: Alkylphenols Category Sponsored Chemical Structures		
CASRN Name	**CASRN**	**Chemical Structure**
p-Dodecylphenol	210555-94-5	
Di- and Tri-Substituted Mixed Alkylphenols		
2,3,6-Trimethylphenol	2416-94-6	
2,4-Di-*tert*-butylphenol	96-76-4	
2,6-Di-*tert*-butylphenol	128-39-2	
2,4-Di-*tert*-pentylphenol	120-95-6	

Table 1: Alkylphenols Category Sponsored Chemical Structures		
CASRN Name	**CASRN**	**Chemical Structure**
4-*sec*-Butyl-2,6-tert-butylphenol	17540-75-9	
2,4,6-Tri-*tert*-butylphenol	732-26-3	
2,4-bis(alpha, alpha-Dimethylbenzyl)phenol	2772-45-4	

1.2 Physical-Chemical Properties

The physical-chemical properties of the alkylphenols category are summarized in Table 2a-c. The alkylphenols are generally solids with the exception of the o-substituted alkyl phenols (CASRN 89-72-5 and 88-18-6) and phenol, 4-dodecyl-, branched (CASRN 210555-94-5), which are liquids, and phenol, 4-nonyl- branched (CASRN 84852-15-3) and phenol, 2,4-bis(1,1-dimethylpropyl)- (CASRN 120-95-6), which have melting points near room temperature. Alkylphenols have low to moderate water solubility except for phenol, 2,3,6-trimethyl- (CASRN 2416-94-6) which has a high water solubility. Vapor pressures range from low to moderate.

2 General Information on Exposure

2.1 Production Volume and Use Pattern

o-Substituted Alkylphenols

The *o*-substituted alkylphenols category chemicals had aggregated production and/or import volumes in the United States between 11 million and 60 million pounds during calendar year 2005. The volumes of the subcategory members were:

- CASRN 88-18-6 1 million to 10 million pounds
- CASRN 89-72-5 10 million to 50 million pounds

Non-confidential information in the IUR indicated that the industrial processing and uses of these chemicals include: intermediates or stabilizers in chemical product and preparation manufacturing; petroleum and coal products manufacturing and petroleum refineries. Non-confidential information in the IUR indicated that the commercial and consumer products containing these chemicals include lubricants, greases and fuel additives. The HPV submission for the *o*-substituted alkylphenols category indicated that CASRN 88-18-6 is used as a starting material for the synthesis of flavor and fragrance chemicals, antioxidants, insecticides, and phenolic resins; and CASRN 89-72-5 is used as a chemical intermediate in the synthesis of insecticides, herbicides and as a polymerization inhibitor. The HSDB states that CASRN 88-18-6 is used as a chemical intermediate for synthetic resins, plasticizers, surface-active agents, and perfumes; as an antioxidant for aviation gasoline; and a starting material for the synthesis of antioxidants and agro chemicals. The HSDB states that CASRN 89-72-5 is used as a chemical intermediate in the production of resins, plasticizers, surface active-agents; and in the syntheses of insecticides, acaricides, and herbicides.

Table 2a. Physical-Chemical Properties of o-Substituted Alkyl Phenols[1]		
Property	**Phenol, 2-(1-methyl propyl)-**	**Phenol, 2-(1,1-dimethyl ethyl)-**
CASRN	89-72-5	88-18-6
Molecular Weight	150.22	150.22
Physical State	Liquid	Liquid
Melting Point	14°C (measured)	-7°C (measured)
Boiling Point	224°C (measured)	223°C (measured)
Vapor Pressure	5×10^{-2} mm Hg at 25°C (estimated)	9.0×10^{-2} mm Hg at 25°C (measured)
Dissociation Constant (pK_a)	10.39 (measured)	9.9–10.9 (estimated)
Henry's Law Constant	1.5×10^{-6} atm-m^3/mol (estimated)[2]	1.5×10^{-6} atm-m^3/mol (estimated)[2]
Water Solubility	$1.7\times10^{+}$ mg/L at 25°C (estimated)	$7\times10^{+2}$ mg/L at 25°C (measured)[2]
Log K_{ow}	3.27 (measured)	3.31 (measured)

[1]Schenectady International. June 9, 2006. Revised Robust Summary and Test Plan for Alkyl Phenols Category. http://www.epa.gov/chemrtk/pubs/summaries/alkylphn/c13007tc.htm.
[2]US EPA. 2008. Estimation Programs Interface Suite™ (version 3.20). United States Environmental Protection Agency, Washington, DC, USA Available online at: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.
[3]Baglay, A.K. et al. J. Chem. Eng. Data 33:512-18 (1988).
[4]The chemical is a complex mixture where the composition may vary.
[5]Hawley C.G. The Condensed Chemical Dictionary, 9th Ed. New York: Van Nostrand Reinhold Co., 1977, p 633.

Table 2b. Physical-Chemical Properties of p-Substituted Alkyl Phenols[1]									
Property	**4-Phenol, (1,1-Dimethyl ethyl)-**	**Phenol, 4-(1-methyl propyl)-**	**Phenol, 4-(1,1-dimethyl propyl)-**	**Phenol, heptyl derivs.**	**4-Phenol, (1,1,3,3-tetramethyl butyl)-**	**4-Phenol, octyl-**	**Phenol, 4-(1-methyl-1-phenyl ethyl)-**	**Phenol, 4-nonyl-, branched**	**Phenol, 4-dodecyl-, branched**
CASRN	98-54-4	99-71-8	80-46-6	72624-02-3	140-66-9	1806-26-4	599-64-4	84852-15-3	210555-94-5
Molecular Weight	150.22	150.22	164.25	192.31	206.33	206.33	212.29	220.36	262.44
Physical State	Solid	Solid	Solid	Solid	Solid	Solid	Solid	Solid/Liquid	Liquid
Melting Point	100°C (measured)	53–62°C (measured)	94–95°C (measured)	No Data[4]	79–82°C (measured)	44-45°C (measured)[5]	72°C (measured)	24.5°C (measured)	-9 °C (measured)
Boiling Point	237°C (measured)	239–241°C (measured)	263°C (measured)	256-280°C (measured)	280–283°C (measured)	296°C (measured)	335°C (measured)	310°C (measured)	308°C (measured)
Vapor Pressure	3.8×10^{-3} mm Hg at 20°C (measured)	3.7×10^{-2} mm Hg at 25°C (measured)	2×10^{-3} mm Hg at 25°C (measured)[2]	8.5×10^{-5} mm Hg at 25°C (measured)	1.6×10^{-3} mm Hg at 20°C (measured)	9.8×10^{-5} mm Hg at 25°C (estimated)	2.3×10^{-5} mm Hg at 25°C (estimated)	3×10^{-5} mm Hg at 25°C (measured)	6.9×10^{-7} mm Hg at 25°C (measured)
Dissociation Constant (pK_a)	10.39 (measured)	9.9–10.9 (estimated)	10.43 (measured)	9.9–10.9 (estimated)	9.9–10.9 (estimated)	9.9–10.9 (estimated)	9.9–10.9 (estimated)	9.9–10.9 (estimated)	9.9–10.9 (estimated)
Henry's Law Constant	1.2×10^{-6} atm-m^3/mol (estimated)[2]	1.5×10^{-6} atm-m^3/mol (estimated)[2]	1.9×10^{-6} atm-m^3/mol (estimated)[2]	3.4×10^{-6} atm-m^3/mol (estimated)[2]	4.5×10^{-6} atm-m^3/mol (estimated)[2]	4.5×10^{-6} atm-m^3/mol (estimated)[2]	8.8×10^{-8} atm-m^3/mol (estimated)[2]	6.0×10^{-6} atm-m^3/mol (estimated)[2]	1.4×10^{-5} atm-m^3/mol (estimated)[2]
Water Solubility	$8\times10^{+2}$ mg/L at 20°C (measured)	$9.6\times10^{+2}$ mg/L at 25°C (measured)	$1.7\times10^{+2}$ mg/L at 25°C (measured)	12.2 mg/L at 25°C (measured)	17–19 mg/L at 22°C (measured)	3.1 mg/L at 25°C (estimated)	84 mg/L at 25°C (estimated)	3.9 mg/L at 25°C (seawater); 1.2 mg/L at 25°C (estimated)	2.1 mg/L at 25°C (measured)
Log K_{ow}	3.31 (measured)	3.08 (measured)	4.03 (measured)	4.5 (measured)	4.12 (measured)	5.5 (estimated)	4.12 (estimated)	3.8–4.77 (measured)	7.1 (measured)

[1]Schenectady International. June 9, 2006. Revised Robust Summary and Test Plan for Alkyl Phenols Category. http://www.epa.gov/chemrtk/pubs/summaries/alkylphn/c13007tc.htm.
[2]US EPA. 2008. Estimation Programs Interface Suite™ (version 3.20). United States Environmental Protection Agency, Washington, DC, USA Available online at: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.
[3]Baglay, A.K. et al. J. Chem. Eng. Data 33:512-18 (1988).
[4]The chemical is a complex mixture where the composition may vary.
[5]Hawley C.G. The Condensed Chemical Dictionary, 9th Ed. New York: Van Nostrand Reinhold Co., 1977, p 633.

Table 2c. Physical-Chemical Properties of Di- and Tri-Substituted Mixed Alkyl Phenols[1]							
Property	**Phenol, 2,3,6-trimethyl-**	**Phenol, 2,4-bis(1,1-dimethyl ethyl)-**	**Phenol, 2,6-bis(1,1-dimethyl ethyl)-**	**Phenol, 2,4-bis(1,1-dimethyl propyl)-**	**Phenol, 2,6-bis(1,1-dimethyethyl)-4-(1-methyl propyl)-**	**Phenol, 2,4,6-tris(1,1-dimethyl ethyl)-**	**Phenol, 2,4-bis(1-methyl-1-phenyl ethyl)-**
CASRN	2416-94-6	96-76-4	128-39-2	120-95-6	17540-75-9	732-26-3	2772-45-4
Molecular Weight	136.19	206.33	206.33	234.38	262.44	262.44	330.47
Physical State	Solid	Solid	Solid	Solid/Liquid	Solid	Solid	Solid
Melting Point	65°C (measured)	56.5°C (measured)	36–37°C (measured)	26°C (measured)	47°C (measured)	131°C (measured)	65°C (measured)
Boiling Point	222°C (measured)	264°C (measured)	253°C (measured)	273°C (measured)[4]	275°C (measured)	278°C (measured)	325°C (measured)[4]
Vapor Pressure	3.5×10^{-2} mm Hg at 25°C (measured)[3]	7.5×10^{-3} mm Hg at 20°C (measured)	7.6×10^{-3} mm Hg at 20°C (measured)	8.4×10^{-5} mm Hg at 25°C (estimated)	1.7×10^{-3} mm Hg at 25°C (estimated)	6.6×10^{-4} mm Hg at 25°C (measured)	6.5×10^{-5} mm Hg at 25°C (estimated)
Dissociation Constant (pK_a)	9.9–10.9 (estimated)	9.9–10.9 (estimated)	9.9–10.9 (estimated)	9.9–10.9 (estimated)	9.9–10.9 (estimated)	9.9–10.9 (estimated)	9.9–10.9 (estimated)
Henry's Law Constant	7.5×10^{-7} atm-m^3/mol (estimated)[2]	3.7×10^{-6} atm-m^3/mol (estimated)[2]	3.7×10^{-6} atm-m^3/mol (estimated)[2]	6.0×10^{-6} atm-m^3/mol (estimated)[2]	9.6×10^{-6} atm-m^3/mol (estimated)[2]	9.6×10^{-6} atm-m^3/mol (estimated)[2]	1.4×10^{-8} atm-m^3/mol (estimated)[2]
Water Solubility	$1.4\times10^{+3}$ mg/L at 25°C (measured)	12 mg/L at 20°C (measured)	4.1 mg/L at pH 7 at 25°C; 3.9 mg/L at pH 4 at 25°C; 4.7 mg/L at pH 9 at 25°C	1.6 mg/L at 25°C (estimated)	0.75 mg/L at 25°C (estimated)	35 mg/L at 25°C (measured)[2]	0.20 mg/L at 25°C (estimated)
Log K_{ow}	2.72 (measured)	5.19 (measured)[3]	4.5 (measured)	6.31 (estimated)	6.43 (estimated)	6.06 (measured)	6.73 (estimated)

[1]Schenectady International. June 9, 2006. Revised Robust Summary and Test Plan for Alkyl Phenols Category. http://www.epa.gov/chemrtk/pubs/summaries/alkylphn/c13007tc.htm.

[2]US EPA. 2008. Estimation Programs Interface Suite™ (version 3.20). United States Environmental Protection Agency, Washington, DC, USA Available online at: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.

[3]Chemicals Inspection and Testing Institute; Biodegradation and bioaccumulation data of existing chemicals based on the CSCL Japan Chemical Industry Ecology – Toxicology and Information Center. ISBN 4-89074-101-1 (1992)

[4]Aldrich; Handbook of Fine Chemicals and Laboratory Equipment. 2000-2001. Milwaukee, WI: Aldrich Chem Co. (2000). For 120-95-6, the extrapolated value is from 169-170 °C at 22 mm Hg. For 2772-45-4, the extrapolated value is from 206°C at 15 mm Hg.

p-Substituted Alkylphenols

The *p*-substituted alkylphenols category chemicals had aggregated production and/or import volumes in the United States between 263 million and 880 million pounds during calendar year 2005. The volumes of the subcategory members were:

- CASRN 98-54-4 50 million to 100 million pounds
- CASRN 99-71-8 1 million to 10 million pounds
- CASRN 80-46-6 1 million to 10 million pounds
- CASRN 72624-02-3 1 million to 10 million pounds
- CASRN 140-66-9 50 million to 100 million pounds
- CASRN 1806-26-4 No 2006 IUR data
- CASRN 599-64-4 10 million to 50 million pounds
- CASRN 84852-15-3 100 million to 500 million pounds
- CASRN 210555-94-5 50 million to 100 million pounds

Non-confidential information in the IUR indicated that the industrial processing and uses of these chemicals include processing as intermediates, stabilizers and "other" in resin and syntheic rubber manufacturing, printing ink manufacturing, and soap and cleaning compound manufacturing. The HPV submission for CASRN 599-64-4 did not contain information on use. The HPV submission for the other alkylphenols category chemicals states that chemicals in the *p*-substituted alkylphenols category are used in fragrances, demulsifiers, biocides, oil field chemicals, surfactants, tackifier resins, ink resins and stabilizers, lube oil additives, co-solvent, as well as intermediates in the synthesis of antioxidants, phenolic resins and oil additives. The HPV submission for CASRN 72624-02-3 states that it is used in manufacturing of lubricant additives. The HSDB states that these chemicals are used in the manufacture of synthetic resins, lubricant additives, various agricultural and pesticide products, fungicides, surfactants, plasticizers, antioxidants, stabilizers, vulcanization agents, dyestuffs, and adhesives; plasticizer, antioxidant, fuel oil stabilizer and fumigant.

Di- and Tri-Substituted Alkylphenols

The di- and tri-substituted mixed alkylphenols category chemicals had aggregated production and/or import volumes in the United States between 182 million and 770 million pounds during calendar year 2005. The volumes of the subcategory members were:

<u>Di-Substituted Alkylphenols:</u>

- CASRN 96-76-4 50 million to 100 million pounds
- CASRN 128-39-2 100 million to 500 million pounds
- CASRN 120-95-6 10 million to 50 million pounds
- CASRN 2772-45-4 1 million to 10 million pounds

<u>Tri-Substituted Alkylphenols:</u>

- CASRN 2416-94-6 1 million to 10 million pounds
- CASRN 17540-75-9 10 million to 50 million pounds
- CASRN 732-26-3 10 million to 50 million pounds

Non-confidential information in the IUR indicated that the industrial processing and uses of these chemicals include processing as intermediates and stabilizers in chemical product and preparation manufacturing, petroleum and coal products manufacturing, plastics product manufacturing, and petroleum refineries. Non-confidential information in the IUR indicated that the commercial and consumer products containing these chemicals include: lubricants, greases and fuel additives, as well as rubber and plastic products. .The HPV submission for the alkylphenols category states that the di- and tri-substituted mixed alkylphenols category chemicals are used as antioxidants; stabilizers for polyols, PVC, polyurethane, adhesives, and functional fluids; and also as intermediates in the manufacture of phenolic antioxidants, UV stabilizers, surfactants, and fuel additives. The HSDB states that these chemicals are primarily used as intermediates, antioxidant, and as starting material for vitamin E.

2.2 Environmental Exposure and Fate

There is potential for environmental releases to various media including water, land and air.

The environmental fate properties of the alklyphenols category are provided in Table 3a-c. The alkylphenols are expected to have low to moderate mobility in soil. In general alkylphenols with lower molecular weight and less branching biodegrade faster while those with higher molecular weight and more complex substituted groups will biodegrade very slowly, therefore the expected range of persistence is moderate (P2) to high (P3). Volatilization of the alkylphenols from water and moist soils is considered low to moderate based on their Henry's Law constants. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered moderate except for phenol, 2,3,6-trimethyl-phenol which is considered rapid. Bioaccumulation potential ranges from low (B1) to high (B3) given the estimated and measured bioconcentration factors for the category members.

Table 3a. Environmental Fate Characteristics of o-Substituted Alkyl Phenols[1]		
Property	**Phenol, 2-(1-methyl propyl)-**	**Phenol, 2-(1,1-dimethyl ethyl)-**
CASRN	89-72-5	88-18-6
Photodegradation Half-life	2.91 hours (estimated)	3.16 hours (estimated)
Biodegradation	0% in 28 days (not readily biodegradable)[3]	No data
Hydrolysis	Stable	Stable
Bioconcentration	BCF = 66 (estimated)[2]; BCF = 16-27 (carp)[3]	BCF = 25 (estimated)[2]
Log K_{oc}	3.42 (estimated)[2]	3.29 (estimated)[2]
Fugacity (Level III Model)		
Air	0.55%	0.31%
Water	24.8%	17%
Soil	74%	81.9%
Sediment	0.69%	0.79%
Persistence[4]	P3	P3[5]
Bioaccumulation[4]	B1	B1

[1]Schenectady International. June 9, 2006. Revised Robust Summary and Test Plan for Alkyl Phenols Category. http://www.epa.gov/chemrtk/pubs/summaries/alkylphn/c13007tc.htm.
[2]US EPA. 2008. Estimation Programs Interface Suite™ (version 3.20). United States Environmental Protection Agency, Washington, DC, USA Available online at: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.
[3]National Institute of Technology and Evaluation. 2002. Biodegradation and Bioconcentration of Existing Chemical Substances under the Chemical Substances Control Law. http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html.
[4]Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.
[5]Persistence levels were estimated by comparing persistence levels with similarly structured chemicals in this group.

Table 3b. Environmental Fate Characteristics of p-Substituted Alkyl Phenols[1]

Property	4-Phenol, (1,1-dimethyl ethyl)-	Phenol, 4-(1-methyl propyl)-	Phenol, 4-(1,1-dimethyl propyl)-	Phenol, heptyl derivs.	4-Phenol, (1,1,3,3-tetramethyl butyl)-	4-Phenol, octyl-	Phenol, 4-(1-methyl-1-phenyl ethyl)-	Phenol, 4-nonyl-, branched	Phenol, 4-dodecyl-, branched
CASRN	98-54-4	99-71-8	80-46-6	72624-02-3	140-66-9	1806-26-4	599-64-4	84852-15-3	210555-94-5
Photodegradation Half-life	3.16 hours (estimated)	2.91 hours (estimated)	3.07 hours (estimated)	2.63 hours (estimated)	3.03 hours (estimated)	2.55 hours (estimated)	2.87 hours (estimated)	2.48 hours (estimated)	2.65 hours (estimated)
Biodegradation	98% in 28 days (die-away test); 0% in 28 days (not readily biodegradable)[3]	67.3% in 28 days (measured); >60% in 10 days (readily biodegradable); 0% in 28 days (not readily biodegradable)[3]	No data	No data	0% in 28 days; 20% in 28 days; 70% in 35 days (not readily biodegradable)[3]	0% in 28 days (not readily biodegradable)[3]	0% in 28 days (not readily biodegradable)[3]	7% in 28 days; 53% in 28 days; 62% in 28 days (not readily biodegradable)	25% in 28 days; 6% in 28 days (not readily biodegradable)
Hydrolysis	Stable	Stable	Stable	Stable	Stable	Stable	Stable	Stable	Stable
Bioconcentration	BCF = 71 (estimated)[2]; BCF = 20-88 (carp)[3]	BCF = 47 (estimated)[2]; BCF = 0.93-37 (carp)[3]	BCF = 206 (estimated)[2]	BCF = 1,429 (estimated)[2]	BCF = 2,303 (estimated)[2]; BCF = 12-469 (carp)[3]	BCF = 341 (estimated)[2]; BCF = 12-469 (carp)[3]	BCF = 298 (estimated)[2]; BCF = 69-190 (carp)[3]	BCF = 5,517 (estimated)[2]	BCF = 11,570 (estimated)[2]
Log K_{oc}	3.28 (estimated)[2]	3.41 (estimated)[2]	3.58 (estimated)[2]	4.26 (estimated)[2]	4.18 (estimated)[2]	4.52 (estimated)[2]	4.65 (estimated)[2]	4.60 (estimated)[2]	5.68 (estimated)[2]
Fugacity (Level III Model) Air Water Soil Sediment	 0.262% 18.4% 80.5% 0.85%	 0.559% 25.1% 73.8% 0.488%	 0.25% 17.1% 79.4% 3.27%	 0.16% 1.07% 96.6% 2.15%	 0.168% 9.07% 53.3% 37.5%	 0.321% 12.4% 48.0% 39.3%	 0.166% 15.1% 80.0% 4.72%	 0.09% 4.5% 36.9% 58.5%	 0.02% 0.008% 97.7% 2.17%
Persistence[4]	P2	P2	P3[5]	P2[5]	P3	P3	P3	P2	P2
Bioaccumulation[4]	B1	B1	B1	B2	B1	B1	B1	B3	B3

[1]Schenectady International. June 9, 2006. Revised Robust Summary and Test Plan for Alkyl Phenols Category. http://www.epa.gov/chemrtk/pubs/summaries/alkylphn/c13007tc.htm.
[2]US EPA. 2008. Estimation Programs Interface Suite™ (version 3.20). United States Environmental Protection Agency, Washington, DC, USA Available online at: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.
[3]National Institute of Technology and Evaluation. 2002. Biodegradation and Bioconcentration of Existing Chemical Substances under the Chemical Substances Control Law. http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html.
[4]Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.
[5]Persistence levels were estimated by comparing persistence levels with similarly structured chemicals in this group.

Table 3c. Environmental Fate Characteristics of Di- and Tri-Substituted Mixed Alkyl Phenols[1]

Property	**Phenol, 2,3,6-trimethyl-**	**Phenol, 2,4-bis(1,1-dimethyl ethyl)-**	**Phenol, 2,6-bis(1,1-dimethyl ethyl)-**	**Phenol, 2,4-bis(1,1-dimethyl propyl)-**	**Phenol, 2,6-bis(1,1-dimethyethyl)-4-(1-methyl propyl)-**	**Phenol, 2,4,6-tris(1,1-dimethyl ethyl)-**	**Phenol, 2,4-bis(1-methyl-1-phenyl ethyl)-**
CASRN	2416-94-6	96-76-4	128-39-2	120-95-6	17540-75-9	732-26-3	2772-45-4
Photodegradation Half-life	0.98 hours (estimated)	2.61 hours (estimated)	2.61 hours (estimated)	2.5 hours (estimated)	6.27 hours (estimated)	8 hours (estimated)	2.24 hours (estimated)
Biodegradation	98% in 14 days (inherently biodegradable) 1% in 28 days (not readily biodegradable)[3] anaerobic 54% in 8 weeks	2% in 28 days (not readily biodegradable); 0% in 28 days (not readily biodegradable)[3]	4% in 28 days; 1% in 28 days; 0% in 56 days (not readily biodegradable)	0% in 28 days (not readily biodegradable)[3]	0% in 28 days (not readily biodegradable)[3]	0% in 28 days (not readily biodegradable)[3]	No data
Hydrolysis	Stable	Stable	Stable	Stable	Stable	Stable	Stable
Bioconcentration	BCF = 23 (estimated)[2]	BCF = 702 (estimated)[2]; BCF = 128-436 (carp)[3]	BCF = 435 (estimated)[2]	BCF = 5,150 (estimated)[2]	BCF = 6,313 (estimated)[2]	BCF = 3,282 (estimated)[2]; BCF = 4320-23200 (carp)[3]	BCF = $1.1\times10^{+4}$ (estimated)[2]
Log K_{oc}	3.08 (estimated)[2]	4.15 (estimated)[2]	4.15 (estimated)[2]	5.74 (estimated)[2]	5.15 (estimated)[2]	5.00 (estimated)[2]	6.90 (estimated)[2]
Fugacity (Level III Model) Air Water Soil Sediment	 0.1% 21.6% 78.1% 0.24%	 0.15% 9.94% 55.8% 34.1%	 0.17% 12.3% 63.9% 23.6%	 0.08% 3.06% 32% 64.8%	 0.12% 2.0% 32.7% 65.1%	 1.65% 2.84% 36.3% 60.7%	 0.03% 1.6% 35% 63.3%
Persistence[4]	P2	P3	P3	P3	P3	P3	P3[5]
Bioaccumulation[4]	B1	B1	B1	B3	B3	B3	B3

[1]Schenectady International. June 9, 2006. Revised Robust Summary and Test Plan for Alkyl Phenols Category. http://www.epa.gov/chemrtk/pubs/summaries/alkylphn/c13007tc.htm.
[2]US EPA. 2008. Estimation Programs Interface Suite™ (version 3.20). United States Environmental Protection Agency, Washington, DC, USA Available online at: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.
[3]National Institute of Technology and Evaluation. 2002. Biodegradation and Bioconcentration of Existing Chemical Substances under the Chemical Substances Control Law. http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html.
[4]Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.
[5]Persistence levels were estimated by comparing persistence levels with similarly structured chemicals in this group.

3 Human Health Hazard

A summary of health effects data submitted for SIDS endpoints is provided in Table 4. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Oral and Dermal Toxicity

o-Substituted Alkylphenols

o-sec-Butylphenol (CASRN 89-72-5)
Sprague-Dawley rats (5/sex/dose) were given a single oral dose of *o-sec*-butylphenol at dose levels ranging from 200 to 5000 mg/kg-bw. Animals were observed for 14 days after dosing and underwent a gross pathological examination. At dose levels of 2000 and 5000 mg/kg-bw/day, animals died within one hour of treatment. The acute oral median LD_{50} value was greater than 200 mg/kg-bw, but less than 2000 mg/kg-bw. Another oral LD_{50} value of 2700 mg/kg-bw was reported for this chemical in the robust summary, but no other details were provided.

2-tert-Butylphenol (CASRN 88-18-6)
(1) Fisher 344 rats (5/sex/dose) were given a single oral dose of 2-*tert*-butylphenol at dose levels of 474, 664, 930, 2551, and 5000 mg/kg-bw. All animals in the two highest dose levels died and 8/10 animals died at the 930 mg/kg-bw dose level. The reported LD_{50} was 789 mg/kg-bw.

(2) Fisher 344 rats (5/sex/dose) were given a single dose of 2-*tert*-butylphenol applied to the skin for 24-hours. Dose levels were 1020, 1420, and 2000 mg/kg-bw in males and 520, 720, 1020, and 2000 mg/kg-bw in females. Dermal LD_{50} values of 1373 mg/kg-bw for males and 705 mg/kg-bw for females were reported.

p-Substituted Alkylphenols

Acute oral toxicity data are available for all members of the *p*-substituted alkylphenols subcategory and acute dermal toxicity data are available for one subcategory member. The oral LD_{50} values range from > 200 to 4000 mg/kg-bw. The dermal LD_{50} value is > 2000 mg/kg-bw. Available LD_{50} values for individual subcategory members are provided in Table 3.

Di- and Tri-Substituted Mixed Alkylphenols

Acute oral toxicity data are available for all but one member of di- and tri-substituted mixed alkylphenols subcategory and acute dermal toxicity data are available for one subcategory member. The oral LD_{50} values range from 920 to > 5000 mg/kg-bw/day. The dermal LD_{50} value is > 1000 mg/kg-bw/day. Available LD_{50} values for individual subcategory members are provided in Table 3.

Repeated-Dose Toxicity

o-Substituted Alkylphenols

Repeated-dose toxicity data were not provided for either member of the of *o*-substituted alkylphenols subcategory: *o-sec*-butylphenol (CASRN 89-72-5) and 2-*tert*-butylphenol (CASRN 88-18-6).

p-Substituted Alkylphenols

p-tert-Butylphenol (CASRN 98-54-4)
(1) In a 14-day range-finding study (for the definitive study below), Sprague-Dawley rats (5/sex/dose) were administered *p-tert*-butylphenol daily via gavage in 0.5% aqueous methyl cellulose at 0, 250, 500 and 1000 mg/kg-bw/day for 14 days. At 1000 mg/kg-bw/day, mortality (3 of 5 females and 1 of 5 males) and decreased body weight were observed. Two females at this dose had difficulty breathing. No signs of toxicity were noted when the animals were necropsied. A dose of 250 mg/kg-bw/day was considered an appropriate dose level for the study described below.

(2) In a combined repeated-dose/reproductive/developmental toxicity screening test, male and female Sprague-Dawley rats (number not specified) were administered *p-tert*-butylphenol via gavage in 0.5% aqueous methyl cellulose at 0, 20, 60 and 200 mg/kg-bw/day. Males were exposed for 44 days; females were exposed from 14 days before mating to day 4 of lactation. No treatment-related changes were observed except noisy respiratory sounds in females of the high-dose group. The authors considered this likely related to irritation of the respiratory tract caused by the gavage administration of the chemical. Plasma albumin levels were decreased in males of the high-dose group.
NOAEL= 200 mg/kg-bw/day (based on no adverse effects observed at the highest dose tested)

(3) Male Syrian Golden hamsters (15) were administered *p-tert*-butylphenol in the diet at 15,000 ppm (approximately 1800 mg/kg-bw/day) for 20 weeks. A control group of 15 males was given basal diet. No other details were provided. At the end of the study, there was a decrease in average body weight (by 5%) and relative liver weights (by 21%). Prominent thickening of the forestomach epithelium was seen with a keratin-like white substance in the posterior and anterior wall adjacent to the esophagus. The severity of the hyperplasia of the forestomach was statistically significant ($p < 0.01$ to $p < 0.001$); however, given that there is no such comparable structure in humans, the significance of this finding is unknown. No abnormal histopathololgical findings were reported in the liver, kidney, cheek pouch, lungs, pancreas and urinary bladder. No other details were provided.
Adverse effects observed at the single dose tested, 15,000 ppm (approximately 1800 mg/kg-bw/day)

p-sec-Butylphenol (CASRN 99-71-8)
Wistar rats (males and females; numbers unspecified in the robust summary) were administered *p-sec*-butylphenol in the diet at 0, 1000, 3000, 10000, and 30000 ppm (estimated to be 0, 50, 150, 500, and 1500 mg/kg-bw/day) for 6, 12, 18, and 24 months. No other details were provided. Clinical signs included diarrhea in both sexes at the highest dose beginning the first week and then increasing gradually. Alopecia on the abdomen was observed in the same group

beginning at week 6. Blood urea nitrogen levels were increased in all groups beginning at month 6; there was no indication in the robust summary if this was dose-related or statistically significantly different from controls. Kidney weights (at the highest dose) and corresponding histological changes (at the two highest doses) were increased in both sexes beginning at month 6. Statistical significance was not reported. Histological changes were also reported in esophagus and forestomach in both sexes at ≥ 10000 ppm beginning at month 6. No other effects were reported and no other details were provided.
LOAEL = 10000 ppm (500 mg/kg-bw/day) (based on effects in the kidney, esophagus and forestomach)
NOAEL = 3000 ppm (150 mg/kg-bw/day)

p-tert-Octylphenol (CASRN 140-66-9)
(1) Albino rats (15/sex/dose) were administered *p-tert*-octylphenol daily at dietary concentrations of 5% (approximately 2500 mg/kg-bw/day) for 3 months. Control animals were fed a basil diet. No effects were seen on survival, growth, food consumption, urinary excretion of glucose and protein, hematological parameters, or organ weights or histopathology.
No adverse effects observed at the single dose tested 5% (approximately 2500 mg/kg-bw/day).

(2) Wistar rats (10/sex/dose) were administered *p-tert*-octylphenol in the diet at 0, 30, 300, and 3000 ppm (estimated to be 0, 1.5, 15, and 150 mg/kg-bw/day) for 90 days. No clinical signs of toxicity were observed. Likewise, no effects on food consumption were reported. At 3000 ppm, a 28% increase in water consumption was observed in females, but not in male rats at any dose group. At this same dose, significant reductions in mean body weight gain in both sexes were observed. Organ weight changes at the highest dose group included the heart (females only), kidneys, testes, and brain. These changes were not reported as being statistically significant nor accompanied by corresponding histopathology. A decrease in hemoglobin and hematocrit (statistical significance not provided) was observed in high-dose females only. No other toxicologically relevant, treatment-related effects were reported.
LOAEL = 3000 ppm (150 mg/kg-bw/day) (based on significant reductions in mean body weight gain)
NOAEL = 300 ppm (15 mg/kg-bw/day)

p-Nonylphenol (CASRN 84852-15-3)
(1) Sprague-Dawley rats (5/sex) were administered *p*-nonylphenol in the diet at 0, 25, 100 and 400 mg/kg-bw/day for 28 days. No other information was provided. No treatment-related effects were seen on survival and clinical signs. At 400 mg/kg-bw/day, animals consumed less food and gained less weight. A decrease in glucose level, and increase in mean urea and cholesterol levels were seen. Kidney, liver and testes weights were increased. Histopathological examination in males revealed hyaline droplet accumulation in the renal proximal tubules, which could be indicative of male-rat specific α-2-μ-globulin, and, therefore, not toxicologically relevant to humans; and minor vacuolation in the periportal hepatocytes in the liver. No such effects were seen in females. No other histopathological findings were reported. Decreased cholesterol levels combined with increased liver weights and liver histopathology could be indicative of liver toxicity, but these effects were not seen in females and without more information, these changes were not considered toxicologically meaningful.
LOAEL = 400 mg/kg-bw/day (based on decreases in body weight gain)
NOAEL = 100 mg/kg-bw/day

(2) Four groups of Sprague-Dawley rats (15/sex/group; control and high-dose group 25/sex) were administered diet containing *p*-nonylphenol at 0, 200, 650 and 2000 ppm (approximately 0, 15, 50 and 150 mg/kg-bw/day) for 90 days (Cunny et al., 1997). The control and high-dose group rats (10 out of 25) were maintained on control diets for 4 weeks after completing the 90-day exposure period (recovery group). Estrus cyclicity, sperm count, motility and morphology were evaluated. There was no effect on survival. A small decrease in body weight and food consumption (<10%) was noted in the 150 mg/kg-bw/day. At week 14, a dose-related increase in kidney weights (within or near historical control values) and a decrease in renal hyaline droplets in males from the high-dose group were seen. Kidney weights showed complete recovery following a 4-week recovery period. According to the authors of the study, since these changes were of small magnitude and there were no corresponding clinical or histopathological changes, the findings of kidney weight alterations were not considered toxicologically meaningful. No changes were seen in estrous cycling, sperm evaluations or effects on endocrine organs.
LOAEL = 2000 ppm (approximately 150 mg/kg-bw/day) (based on minor findings of small decreases in body weight).
NOAEL= 650 ppm (approximately 50 mg/kg-bw/day)

Di- and Tri-Substituted Mixed Alkylphenols

***2,6-Di-tert-butylphenol* (CASRN 128-39-2)**
Wistar rats (5/sex/dose) were administered *2,6-di- tert*-butylphenol via gavage at 0, 15, 100 and 600 mg/kg-bw/day for 28 days. At 600 mg/kg-bw/day, serum urea level was decreased in females. An increase in serum total protein level (males and females) and increased serum albumin level (males) were also seen. Enlarged cecum (a pouch connected to the ascending colon of the large intestine and the ileum) was noted in 4/5 males and 5/5 females. Enlarged liver and kidneys were also noted with increased liver weights in males and females and increased kidney weights in males (absolute/relative not specified). A slight increase in the incidence of hepatocellular hypertrophy in the centrilobular area in males and females and eosinophilic inclusions in the renal cortex of males were observed. At 100 mg/kg-bw/day, increased relative liver weights and enlarged cecum were noted in males. No other effects were reported. No other details were provided (including statistical significance) for any of these effects.
LOAEL = 600 mg/kg-bw/day (based on increase liver weight with corresponding histopathology)
NOAEL = 100 mg/kg-bw/day

***2,4,6-Tri-tert-butylphenol* (CASRN 732-26-3)**
Male and female Wistar rats (40/sex/dose) were administered *2,4,6-tri-tert*-butylphenol in the diet at 0, 30, 100, 300 and 1000 ppm (approximately 0, 1.5, 5, 15 and 50 mg/kg-bw/day) for 24 months. At 1000 ppm, a significant reduction in body weight gain was noted in females. Hematological changes, indicative of microcystic anemia were seen (decrease of hemoglobin, mean corpuscular volume) at all intervals in the 300 and 1000 ppm group animals. Marked increases were seen in total cholesterol levels, and gamma glutamyl transpeptidase and glutaryl oxaloacetate transaminase activity at 300 and 1000 ppm at 6- and 12-month intervals. A marked decrease in gamma glutamyl transpeptidase was seen at 18- and 24-month intervals. Increases in relative liver (male and female at 300 and 1000 ppm) and kidney weights (relative/absolute not specified; male and female at 100, 300, and 1000 ppm) and an increase in adrenal weights

(absolute/relative not specified; male and female: swelling, focal necrosis and vacuolization of liver cells at 300 and 1000 groups) were reported. No statistically significant neoplastic lesions were observed in any organs throughout the study. The study authors concluded that the focal necrosis, swelling and vacuolization of liver cells; increases in liver weight; and slight microcytic anemia; and elevation of serum phospholipid and cholesterol levels observed at doses ≥15 mg/kg-bw/day, (that were reported to be more pronounced in females than in males), were indicative of liver toxicity.
LOAEL = 300 ppm (approximately 15 mg/kg-bw/day; based on liver toxicity)
NOAEL = 100 ppm (approximately 5 mg/kg-bw/day)

Reproductive Toxicity

o-Substituted Alkylphenols

Reproductive toxicity information were not provided for either member of the *o*-substituted alkylphenols subcategory, or for *o-sec*-butylphenol (CASRN 89-72-5) and *2-tert*-butylphenol (CASRN 88-18-6); either in the form of one or multi-generation reproductive toxicity studies or repeated-dose toxicity tests that evaluated reproductive organs.

p-Substituted Alkylphenols

p-tert-Butylphenol (CASRN 98-54-4)
In a combined repeated-dose/reproductive/developmental toxicity screening test previously described, male and female rats were administered *p-tert*-butylphenol via gavage in 0.5% aqueous methyl cellulose at 0, 20, 60 and 200 mg/kg-bw/day. Males were exposed to the test substance or 44 days and females from 14 days before mating to day 4 of gestation. No treatment-related changes were observed except noisy respiratory sound in females of the high-dose group. In males of the high-dose group, only plasma albumin level was decreased. There were no treatment related toxic effects on pregnant and lactating females or their offspring.
NOAEL = 200 mg/kg-bw/day (based on no adverse effects observed at the highest dose tested)

p-tert-Octylphenol (CASRN 140-66-9)
In a two-generation reproductive toxicity study by Tyl et al. (1999), Sprague-Dawley rats (30/sex/group) were administered *p-tert*-octylphenol in the diet at 0, 0.2, 20, 200 and 2000 ppm (approximately 0, 0.01, 1, 10 and 100 mg/kg-bw/day for males and 0, 0.015, 1.5, 15 and 150 mg/kg-bw/day for females). Effects related to dietary administration of *p-tert*-octylphenol for two generations in adult animals were limited to minimal reductions in adult body weight, body weight gain, and feed consumption in the high-dose group of 2000 ppm. There were no treatment-related effects on extensive reproductive parameters, testes, prostate, or ovary weight or morphology, on sperm counts, motility, morphology, production, or on estrous cyclicity. Effects in offspring occurred only at the high-dose group of 2000 ppm and were limited to reductions in pup body weights and several minor, transient organ weight differences in weanlings. The reduced pup body weights occurred only during the latter part of lactation when the pups were self-feeding and were therefore not being directly exposed to the test compound by daily dietary ingestion. Since organ weight differences were not observed in adult animals from the same generation and from the same litters, and since there were no correlated functional or histological alterations, the study authors concluded these changes to be of minimal or no toxicological relevance. Slight increases in the time-to-acquisition of developmental landmarks

in female and male pups (vaginal opening and preputial separation) were also observed in the high-dose group. These delays were less than 2 days and were considered by the study authors to be related to the lower body weight, starting late in lactation and continuing through the postweaning exposure periods.
LOAEL (adult systemic toxicity) = 2000 ppm (approximately 100 mg/kg-bw/day for males and 150 for females mg/kg-bw/day; based on effects on body weights**)**
NOAEL (adult systemic toxicity) = 200 ppm (approximately 10 mg/kg-bw/day for males and 15 mg/kg-bw/day for females)
NOAEL (adult reproductive toxicity) = 2000 ppm (approximately 100 mg/kg-bw/day for males and 150 for females mg/kg-bw/day; based on no effects at highest dose tested**)**
LOAEL (offspring toxicity) = 2000 ppm (approximately 150 mg/kg-bw/day for weanlings; based on effects on body weights and delays in acquisition of vaginal opening and preputial separation**)**
NOAEL (offspring toxicity) = 200 ppm (approximately 15 mg/kg-bw/day for weanlings)

p-Nonylphenol (CASRN 84852-15-3)
In a three-generation reproductive toxicity study, Sprague-Dawley rats (30/sex/dose) were administered a diet containing 0, 200, 650 and 2000 ppm (approximately 0, 13-19, 43-64, and 274-322 mg/kg/day) *p*-nonylphenol from study day 1 until necropsy (NTP Report # RACB94021). Premating exposure for F_0 generation was 6 weeks. F_1 and F_2 generation animals received diet containing the same dose after weaning (on postnatal day 21) as their parents. Generations were raised until mating at sexual maturity (approximately postnatal day 86). Adult toxicity was manifested as reductions in terminal body weights at 650 ppm in F_2 males (8%) and F_1 females (7%) and on post-natal days 55-58 in F_3 females (10%) and at 2000 ppm in F_1 female (9%), F_2 (7%), and post-natal day 55-58 F_3 (7%) males and F_0 (9%), F_1 (12%), F_2 (10%), and post-natal day 55-58 F_3 (11%) females. Increased relative kidney weights were observed at 650 ppm and/or 2000 ppm in adult males from the F_0, F1, and F_2 generations and in the F_1 2000 ppm adult females. A treatment-related increase in the incidence of renal tubular degeneration/dilatation was seen in the 200, 650, and 2000 ppm males from all generations and in the 2000 ppm females from the F_1, F_2, and F_3 generations and in the 200 and 650 ppm females in the F_3 generation. Feed consumption, clinical observations, and mortality were not adversely affected. Reproductive changes were seen in both male and female adults at or above 650 ppm based on decreased epididymal sperm density and testicular sperm head counts in males, and increased estrous cycle length and decreased ovarian weights observed in females. Vaginal opening in pups was accelerated by 1.5-7.3 days at 650 ppm and by 2.9-6.0 days at 2000 ppm, in all three generations. The acceleration in vaginal opening was taken as indication of the estrogenicity of the test substance. No treatment-related changes were noted in the litter data for the remaining reproductive/developmental parameters from all three mating trials including pregnancy index, mating index, proportion of pups born alive, sex ratio, pup weights, anogenital distance, testicular decent, preputial separation, and pup survival.
LOAEL (adult systemic toxicity) = 650 ppm (approximately 43-64 mg/kg-bw/day; based on decreased body weight**)**
NOAEL (adult systemic toxicity) = 200 ppm (approximately 13-19 mg/kg-bw/day)
LOAEL (adult reproductive toxicity) = 650 ppm (approximately 43-64 mg/kg-bw/day; based on decreased epididymal sperm density and testicular sperm head counts in males, and increased estrous cycle length and decreased ovarian weights in females**)**
NOAEL (adult reproductive toxicity) = 200 ppm (approximately 13-19 mg/kg-bw/day)

LOAEL (offspring toxicity) = 650 ppm (approximately 43-64 mg/kg-bw/day; based on accelerated vaginal opening in pups**)**
NOAEL (offspring toxicity) = 200 ppm (approximately 13-19 mg/kg-bw/day)

Di- and Tri-Substituted Mixed Alkylphenols

2,6-Di-tert-butylphenol (CASRN 128-39-2)
In a combined reproductive and developmental toxicity screening test, Wistar rats (10/sex/dose) were administered 0, 30, 150 and 750 mg/kg-bw/day *2,6-di-tert*-butylphenol by gavage. Animals were dosed throughout the pre-mating and mating period—males received the test substance for a total of 43 days; females up to postnatal day 4. In adult animals, a slight body weight reduction was seen in male and female rats at 750 mg/kg-bw/day; increased food consumption was seen in males and decreased food consumption in females (statistical significance not provided). The robust summary also indicates 'severe toxic symptoms' were observed in adult animals, but no other details were provided. An increased reduced pup viability index (measured on either lactation day 4 or 21) was seen for females at 750 mg/kg-bw/day. According to the robust summary, differences in study summaries exist between the primary reference and the transcribed secondary reference for this study. In the primary reference (not reviewed for this hazard characterization), reductions in pup weight gain at 750 mg/kg-bw/day were noted, but no other details were provided. This was not mentioned in the secondary reference for this study. The robust summary did not report any other effects on reproductive or developmental parameters. There were no effects noted on macroscopic or microscopic examination.
LOAEL (adult systemic toxicity) = 750 mg/kg-bw/day (based on marginal effects on body weight in adult animals)
NOAEL (reproductive toxicity) = 750 mg/kg-bw/day
LOAEL (developmental toxicity) = 750 mg/kg-bw/day (based on reduced viability and weight gain in pups)
NOAEL (adult systemic/developmental toxicity) = 150 mg/kg-bw/day

Developmental Toxicity

o-Substituted Alkylphenols

Prenatal developmental toxicity data were not provided for either member of the of *o*-substituted alkylphenols subcategory, or for *o-sec*-butylphenol (CASRN 89-72-5) and 2-*tert*-butylphenol (CASRN 88-18-6).

p-Substituted Alkylphenols

p-tert-Butylphenol (CASRN 98-54-4)
In a combined repeated-dose/reproductive/developmental toxicity screening test previously described, male and female rats were administered *p-tert*-butylphenol via gavage in 0.5% aqueous methyl cellulose at 0, 20, 60 and 200 mg/kg-bw/day. Males were exposed to the test substance or 44 days and females from 14 days before mating to day 4 of gestation. No treatment-related changes were observed except noisy respiratory sound in females of the high-doe group. In males of the high-dose group, only plasma albumin level was decreased. There were no treatment related toxic effects on pregnant and lactating females or their offspring.
NOAEL (maternal/developmental toxicity)= 200 mg/kg-bw/day (based on no adverse effects observed at the highest dose tested)

p-Nonylphenol (CASRN 84852-15-3)
Pregnant female Wistar rats (number unspecified) were administered *p*-nonylphenol via gavage at 0, 75, 150 and 300 mg/kg-bw/day during days 6-15 of gestation. At 150 mg/kg-bw/day, 3 of 21 females showed pale and irregularly shaped kidneys, reddening of the renal pelvis and small spleens. At 300 mg/kg-bw/day, increased mortality, reduced body weight gain and food consumption and kidney and spleen effects were observed. There were no marked differences between groups in the mean number and presentation of the fetuses, left and right intra-uterine distribution, sex ratio, fetal and placental weights, number of runts and dead fetuses, resorptions, implantations and corpora lutes indices. No malformation or abnormalities were seen in fetuses.
LOAEL (maternal toxicity) = 150 mg/kg-bw/day (based on kidney and spleen effects)
NOAEL (maternal toxicity) = 75 mg/kg-bw/day
NOAEL (developmental toxicity) = 300 mg/kg-bw/day (highest dose tested)

Di- and Tri-Substituted Mixed Alkylphenols

2,6-Di-tert-butylphenol (CASRN 128-39-2)
In a combined reproductive and developmental toxicity screening test, Wistar rats (10/sex/dose) were administered 0, 30, 150 and 750 mg/kg-bw/day *2,6-di-tert*-butylphenol by gavage (previously described).
LOAEL (adult systemic toxicity) = 750 mg/kg-bw/day (based on marginal effects on body weight in adult animals)
LOAEL (developmental toxicity) = 750 mg/kg-bw/day (based on reduced viability index and weight gain in pups)
NOAEL (adult systemic and developmental toxicity) = 150 mg/kg-bw/day

Genetic Toxicity – Gene Mutation

o-Substituted Alkylphenols

o-sec-Butylphenol (CASRN 89-72-5)
The mutagenicity potential of *o-sec*-butylphenol was evaluated *in vitro* in *Salmonella typhimurium* (TA100, TA1535, TA98, and TA1537) in the presence and absence of metabolic activation up to166 μg/plate of the test substance. No increases in mutation frequency were

reported at any concentration tested with or without metabolic activation. Positive controls gave the appropriate response.
***o-sec*-Butylphenol was not mutagenic in this assay.**

2-tert-Butylphenol (CASRN 88-18-6)
The mutagenicity potential of 2-*tert*-butylphenol was evaluated *in vitro* in *S .typhimurium* (TA100, TA1535, TA98, TA 1538 and TA1537) and *E. coli* in the presence and absence of metabolic activation up to 5000 µg/plate of the test substance. No increases in mutation frequency were reported at any concentration tested with or without metabolic activation. Positive controls gave the appropriate response.
2-*tert*-Butylphenol was not mutagenic in this assay.

p-Substituted Alkylphenols

p-tert-Butylphenol (CASRN 98-54-4)
The mutagenicity potential of *p-tert*-butylphenol was evaluated in multiple studies; several *in vitro* in *S. typhimurium* (TA100, TA1535, TA98, TA 1538 and TA1537) and/or *E. coli* assays and several mammalian cell line assays in the presence and absence of metabolic activation up to 4000 µg/plate of test substance. No increases in mutation frequency were reported at any concentration tested with or without metabolic activation. Positive controls gave the expected increase in the number of revertants.
***p-tert*-Butylphenol was not mutagenic in this assay.**
p-sec-Butylphenol (CASRN 99-71-8)
The mutagenicity potential of *p-sec*-butylphenol was evaluated in an Ames test. No other details were provided except the results.
***p-sec*-Butylphenol was not mutagenic in this assay.**

p-tert-Amylphenol (CASRN 80-46-6)
The mutagenicity potential of *p-tert*-amylphenol was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and/or *E. coli* in the presence and absence of metabolic activation at concentrations up to 5000 µg/plate of test substance. No increases in mutation frequency compared with solvent control were reported at any concentration tested with or without metabolic activation.
***p-tert*-Amylphenol was not mutagenic in this assay.**

Heptyl derivatives (p-heptylphenol) (CASRN 72624-02-3)
The mutagenicity potential of heptyl derivatives (*p*-heptylphenol) was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and/or *E. coli* in the presence and absence of metabolic activation at concentrations up to 500 µg/plate of test substance. No increases in mutation frequency compared with a solvent control were reported at any concentration tested with or without metabolic activation. Positive controls gave the expected increase in the number of revertants.
***p*-Heptylphenol was not mutagenic in this assay.**

p-tert-Octylphenol (CASRN 140-66-9)
The mutagenicity potential of *p-tert*-octylphenol was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) in the presence and absence of metabolic activation up to 500 µg/plate of test substance. No increases in mutation frequency were reported at any

concentration tested with or without metabolic activation. No other information was provided in the robust summary.
***p-tert*-Octylphenol was not mutagenic in this assay.**

p-(alpha, alpha-Dimethylbenzyl)phenol (CASRN 599-64-4)
The mutagenicity potential of *p*-(alpha, alpha-dimethylbenzyl)phenol was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) in the presence and absence of metabolic activation up to 500 µg/plate of test substance. No increases in mutation frequency were reported at any concentration tested with or without metabolic activation. Cytotoxicity was observed at concentrations greater than µg/plate with metabolic activation and greater than 50 µg/plate without metabolic activation. No other information was provided in the robust summary.
***p*-(alpha, alpha-Dimethylbenzyl)phenol was not mutagenic in this assay.**

p-Nonylphenol (CASRN 84852-15-3)
The mutagenicity potential of *p*-nonylphenol was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and a mammalian cell line (V79 Chinese hamster cells) in the presence and absence of metabolic activation up to 500 µg/plate of test substance. No increases in mutation frequency were reported at any concentration tested with or without

metabolic activation. No other information was provided in the robust summary.
***p*-Nonylphenol was not mutagenic in these assay.**

Di- and Tri-Substituted Mixed Alkylphenols

Data are not available for 2, 4-di-*tert*-butylphenol (CASRN 96-76-4), 2,4-di-*tert*-pentylphenol (CASRN 120-95-6), 2,4,6-tri-*tert*-butylphenol (CASRN 732-26-3) and 2,4-di-cumylphenol (CASRN 2772-45-4). The data for the tested members of the sub category are extrapolated/interpolated to the untested members of this category.

2,3,6-Trimethylphenol (CASRN 2416-94-6)
The mutagenicity potential of 2,3,6-trimethylphenol was evaluated *in vitro* in *S. typhimurium* (TA100, TA1535, TA98, TA 1538 and TA1537) in two separate experiments in the presence and absence of metabolic activation at up to either 1500 or 5000 µg/plate of test substance. No increases in mutation frequency were reported at any concentration tested with or without metabolic activation. No other information was provided in the robust summary.
2,3,6-Trimethylphenol was not mutagenic in these assays.

2,6-Di- tert-butylphenol (CASRN 128-39-2)
The mutagenicity potential of 2,6-di-*tert*-butylphenol was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and *E. coli* and mammalian cell lines in the presence and absence of metabolic activation at various concentrations of the test substance. No increases in mutation frequency were reported at any concentration tested with or without metabolic activation. Positive controls were stated to be used in one of the two reported bacterial assays.
2,6-Di-*tert*-butylphenol was not mutagenic in these assays.

4-sec-Butyl-2,6-tert-butylphenol (CASRN 17540-75-9)
The mutagenicity potential of 4-*sec*-butyl-2,6-tert-butylphenol was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and *E. coli* in the presence and absence of metabolic activation up to 5000 µg/plate of test substance. No increases in mutation frequency were reported at any concentration tested with or without metabolic activation. Positive controls gave the expected increase in the number of revertants.
4-*sec*-Butyl-2,6-*tert*-butylphenol was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

o-Substituted Alkylphenols

No chromosomal aberration data were provided for either of the members of the of *o*-substituted alkylphenols subcategory: *o-sec*-butylphenol (CASRN 89-72-5) and 2-*tert*-butylphenol (CASRN 88-18-6).

p-Substituted Alkylphenols

Data are not available for *p-tert*-amylphenol (CASRN 80-46-6), *p*-heptylphenol (CASRN 72624-02-3), *p-tert*-octylphenol (CASRN 140-66-9), *p*-octylphenol (CASRN 1806-26-4), *p*-cumylphenol (CASRN 599-64-4), and *p*-dodecylphenol (CASRN 210555-94-5). The data for the tested members of the sub category are extrapolated/interpolated to the untested members.

p-tert-Butylphenol (CASRN 98-54-4)
In vitro chromosomal aberration testing was conducted in Chinese hamster lung cells (CHL) with *p-tert*-butylphenol (up to 0.05 mg/ml) and without (up to 0.08 mg/ml) metabolic activation. Cytotoxicity was observed only in the without activation group and only at the highest concentration. Appropriate responses were seen for negative and positive controls. The test substance induced chromosomal aberrations only in cells which were metabolically activated.
***p-tert*-Butylphenol induced chromosomal aberrations in cells that were metabolically activated, but not in cells without metabolic activation in this assay.**

p-sec-Butylphenol (CASRN 99-71-8)
In vitro chromosomal aberration testing was conducted in Chinese Hamster Lung cells with *p-sec*-butylphenol with and without metabolic activation. The concentration range was up to 5 mg/mL. Appropriate responses were seen for negative and positive controls. The test substance did not induce chromosomal aberrations in cells exposed with or without metabolic activation.
***p-sec*-Butylphenol did not induce chromosomal aberrations in this assay.**

Di- and Tri-Substituted Mixed Alkylphenols

Data are not available for 2,4-di-*tert*-butylphenol (CASRN 96-76-4); 2,4-di-*tert*-pentylphenol (CASRN 120-95-6); 2,4,6-tri-*tert*-butylphenol (CASRN 732-26-3); 2,3,6-Trimethylphenol (CASRN 2416-94-6); and 2,4-di-cumylphenol (CASRN 2772-45-4). The data for the tested members of the sub category are extrapolated/interpolated to the untested members.

2,6-Di- tert-butylphenol (CASRN 128-39-2)
In vitro chromosomal aberration testing was conducted in Chinese Hamster V79 cells with the test substance with and without metabolic activation. The concentration range was up to 6 µg/mL (without activation) and up to 30 µg/mL (with activation). The test substance did not induce chromosomal aberrations in cells exposed with or without metabolic activation. No other information was provided in the robust summary.
***2,6-Di- tert*-butylphenol did not induce chromosomal aberrations in this assay.**

4-sec-Butyl-2,6-tert-butylphenol (CASRN 17540-75-9)
In vitro chromosomal aberration testing was conducted in Chinese Hamster Ovary cells with 4-*sec*-butyl-2,6-*tert*-butylphenol with and without metabolic activation. The concentration range was up to 675 µg/mL. Appropriate responses were seen for negative and positive controls. The test substance did not induce chromosomal aberrations in cells exposed with or without metabolic activation. The test substance is considered negative for chromosomal aberrations with and without metabolic activation.
4-*sec*-Butyl-2,6-*tert*-butylphenol did not induce chromosomal aberrations in this assay.
Genetic Toxicity – Other

p-Substituted Alkylphenols

p-Nonylphenol (CASRN 84852-15-3)
p-Nonylphenol was evaluated in an *in vivo* micronucleus test conducted with NMRI mice (5/sex/dose). A single dose of 500 mg/kg (maximum tolerated dose) was used. The test substance did not demonstrate any mutagenic potential in this *in vivo* system.
***p*-Nonylphenol was not mutagenic in this assay.**

Additional Information

Irritation

Multiple tests were reported in the robust summaries and the results are provided in Table 3.

Sensitization

p-tert-butylphenol (CASRN 98-54-4)
(1) A guinea pig maximization test was conducted in male guinea pigs (number not specified). Three pairs of intracutaneous injections of a 0.5% solution of *p-tert*-butylphenol were given on the bare skin of the shoulder region in male guinea pigs for one week. Filter paper with a 10% solution of *p-tert*-butylphenol was placed onto the shoulder region on top of the injections and held in place by an occlusive patch for 48 hours. Assessment took place 48 and 72 hours after administration.
***p-tert*-butylphenol did cause skin sensitization in guinea pigs.**

(2) White female guinea pigs (20) were painted daily on the bare skin behind their ears with one drop of a 30% solution of a *p-tert*-butylphenol for three weeks followed by a two week rest period, and with a 1% solution of *p-tert*-butylphenol behind the left nipple. Assessment was conducted after 48 hours. Some sensitization to *p-tert*-butylphenol was observed.
***p-tert*-butylphenol caused equivocal skin sensitization in guinea pigs.**

p-tert-Octylphenol (CASRN 140-66-9)
In a skin sensitization study in guinea pigs (20) with a 20% solution of *p-tert*-octylphenol, 0/20 animals showed sensitization 24 or 48 hours after the patch test.
***p-tert*-octylphenol did not cause skin sensitization in guinea pigs.**

p-Nonylphenol (CASRN 84852-15-3)
The results of several guinea pig maximization tests suggest that nonylphenol does not have significant skin sensitizing potential.

Carcinogenicity

***2,4,6-Tri-tert-butylphenol* (CASRN 732-26-3)**
In the 24-month study in rats described above under the repeated-dose toxicity section for the di- and tri-substituted alkylphenols, it was reported that there was no evidence of cancer in the treated animals.

Conclusion:

o-Substituted Alkylphenols

The acute toxicity is low by the oral route and moderate by the dermal route. Repeated-dose, reproductive, and developmental toxicity studies were not available for either member of the *o*-substituted alkylphenols subcategory (CASRNs 89-72-5 and 88-18-6). Members of this alkylphenols subcategory did not induce gene mutations in bacteria. Evaluation of chromosomal effects were not available for either member of this subcategory. Members of this subcategory are considered highly irritating or corrosive to the skin and irritating to eye.

p-Substituted Alkylphenols

The acute toxicity is low by the oral and dermal routes. A combined repeated-dose/reproductive/developmental toxicity study by the oral route with CASRN 98-54-4 in rats showed a NOAEL for systemic toxicity of 200 mg/kg-bw/day (highest dose tested). In a 20-week repeated dose study with the same chemical in male hamsters, decreased body weight and liver weight, and forestomach hyperplasia were observed at the only dose tested (1800 mg/kg-bw/day). A repeated-dose toxicity study by the oral route in rats with CASRN 99-71-8 showed effects in the kidney, esophagus, and forestomach at a dose of 500 mg/kg-bw/day; the NOAEL was 150 mg/kg-bw/day. A repeated-dose toxicity study by the oral route in rats with CASRN 140-66-9 showed a NOAEL for systemic toxicity of 15 mg/kg-bw/day and a LOAEL of 150 mg/kg-bw/day (based on reductions in body weight gain). Two separate 28- and 90-day repeated-dose toxicity studies by the oral route in rats with CASRN 84852-15-3 showed decreases in body weight gain at 400 and 150 mg/kg-bw/day, respectively; the NOAEL for systemic toxicity was 100 and 50 mg/kg-bw/day, respectively. However, a multi-generation study (reported below) with the same chemical showed similar systemic toxic effects (decreases in body weight) at lower doses (43-64 mg/kg-bw/day) in adult animals. The combined repeated-dose/reproductive/developmental toxicity study with CASRN 98-54-4 by the oral route in rats showed no adult/reproductive/or developmental toxicity; the NOAEL for all effects was the highest tested dose of 200 mg/kg-bw/day. A two-generation reproductive toxicity study by the

oral route in rats with CASRN 140-66-9 showed effects on body weights in adults at a dose of 100 mg/kg-bw/day; the NOAEL for adult systemic toxicity was 10 mg/kg-bw/day. There was no evidence of reproductive toxicity in this study and the NOAEL was 100 mg/kg-bw/day for males and 150 mg/kg-bw/day for females. In this same study, there was developmental toxicity at 150 mg/kg-bw/day as demonstrated by effects on pup body weights and delays in acquisition of vaginal opening and preputial separation; the NOAEL for developmental toxicity was 15 mg/kg-bw/day. A three-generation reproductive toxicity study by the oral route in rats with CASRN 84852-15-3 showed decreases in adult body weight at 43-64 mg/kg-bw/day; the NOAEL for systemic toxicity was 13-19 mg/kg-bw/day. This same study showed decreases in epididymal sperm density and testicular sperm head counts in males, and increased estrous cycle length and decreased ovarian weights in females at 43-64 mg/kg-bw/day; the NOAEL for reproductive toxicity was 13-19 mg/kg-bw/day. There was evidence of developmental toxicity in this study as demonstrated by acceleration in the vaginal opening in pups at 43-64 mg/kg-bw/day; the NOAEL for developmental toxicity was 13-19 mg/kg-bw/day. A prenatal developmental toxicity study in rats by the oral route with CASRN 84852-15-3 showed evidence of maternal toxicity as demonstrated by kidney and spleen effects in the dams at 150 mg/kg-bw/day; the NOAEL for maternal toxicity was 75 mg/kg-bw/day. There was no evidence of developmental toxicity in this study and the NOAEL was 300 mg/kg-bw/day. Members of this alkylphenols subcategory did not induce gene mutations in bacteria and did not induce chromosomal aberrations when tested *in vitro* or *in vivo*. Many members of this subcategory are considered highly irritating or corrosive to the skin and irritating to eye.

Di- and Tri-Substituted Alkylphenols

The acute toxicity is low by the oral route and moderate by the dermal route. A repeated-dose toxicity study by the oral route in rats with CASRN 128-39-2 showed increases in liver weight with corresponding histopathology at 600 mg/kg-bw/day; the NOAEL for systemic toxicity was 100 mg/kg-bw/day. A two-year repeated-dose toxicity study in rats by the oral route with CASRN 732-26-3 showed evidence of liver toxicity at 15 mg/kg-bw/day; the NOAEL for systemic toxicity was 5 mg/kg-bw/day. A combined reproductive and developmental toxicity screening study by the oral route in rats with limited postnatal evaluations with CASRN 128-39-2 showed marginal effects on body weights in adults and reduced viability and weight gain in the pups at 750 mg/kg-bw/day; the NOAEL for adult systemic and developmental toxicity was 150 mg/kg-bw/day. There was no evidence of reproductive toxicity in this study and the NOAEL was 750 mg/kg-bw/day. Members of this alkylphenols subcategory did not induce gene mutations in bacteria and did not induce chromosomal aberrations when tested *in vitro* or *in vivo*. Many members of this subcategory are considered moderately irritating to the skin. The two-year repeated-dose toxicity study in rats with CASRN 732-26-3 found no evidence of cancer.

Table 4. Summary Table of the Screening Information Data Set as Submitted under the U.S. Challenge Program: Summary of Human Health Data for Aklylphenols Category

Chemical	Acute Oral Toxicity LD_{50} (mg/kg-bw)	Acute Dermal Toxicity LD_{50} (mg/kg-bw)	Repeated-Dose Toxicity NOAEL/LOAEL (mg/kg-bw/day)	Reproductive Toxicity NOAEL/LOAEL (mg/kg-bw/day)	Developmental Toxicity NOAEL/LOAEL (mg/kg-bw/day) Maternal toxicity	Developmental Toxicity NOAEL/LOAEL (mg/kg-bw/day) Developmental toxicity
***o-sec*-Butylphenol (CASRN 89-72-5)**	**> 200 & < 2000 2700**	No Data 1373 705 (RA)	No Data	No Data	No Data	No Data
2-*tert*-Butylphenol (CASRN 88-18-6)	**789**	**1373 705**	No Data	No Data	No Data	No Data
***p-tert*-Butylphenol (CASRN 98-54-4)**	**> 2000 4000 3620 5360**	No Data > 2000 (RA)	**NOAEL = 200 (rat)**	**NOAEL = 200**	**NOAEL = 200**	**NOAEL = 200**
***p-sec*-Butylphenol (CASRN 99-71-8)**	**1650**	No Data > 2000 (RA)	**NOAEL ~ 150 LOAEL ~ 500**	No Data NOAEL = 200 (RA)	No Data NOAEL = 200 (RA)	No Data NOAEL = 200 (RA)
***p-tert*-Amylphenol (CASRN 80-46-6)**	**1830**	No Data > 2000 (RA)	No Data NOAEL ~ 150 LOAEL ~ 500 (RA)	No Data NOAEL = 200 (RA)	No Data NOAEL = 200 (RA)	No Data NOAEL = 200 (RA)
Heptyl derivatives (*p*-heptylphenol) (CASRN 72624-02-3)	**> 200 & < 2000**	**> 2000**	No Data NOAEL = 10-15 LOAEL = 100-150 (RA)	No Data NOAEL = 200 (RA)	No Data NOAEL = 200 (RA)	No Data NOAEL = 200 (RA)
***p-tert*-Octylphenol (CASRN 140-66-9)**	**2200**	**> 2000**	**NOAEL = 10-15 LOAEL = 100-150**	**NOAEL = 100-150 LOAEL = Not established**	No Data NOAEL = 75 LOAEL = 150 (RA)	**NOAEL = 80 LOAEL = 800**
***p*-Octylphenol (CASRN 1806-26-4)**	**1200**	No Data > 2000 (RA)	No Data NOAEL = 10-15 LOAEL = 100-150 (RA)	No Data NOAEL = 100-150 LOAEL = Not established (RA)	No Data NOAEL = 75 LOAEL = 150 (RA)	No Data NOAEL = 80 LOAEL = 800 (RA)
***p*-(alpha, alpha-Dimethylbenzyl)phenol or *p*-cumylphenol (CASRN 599-64-4)**	**1770**	No Data > 2000 (RA)	NOAEL = 13-19 LOAEL = 43-65 (RA)	No Data NOAEL = 13-19 LOAEL = 43-64 (RA)	No Data NOAEL = 75 LOAEL = 150 (RA)	No Data NOAEL = 80 LOAEL = 800 (RA)
***p*-Nonylphenol (CASRN 84852-15-3)**	**1882**	No Data > 2000 (RA)	**NOAEL = 13-19 LOAEL = 43-65**	**NOAEL = 13-19 LOAEL = 43-64**	**NOAEL = 75 LOAEL = 150**	**NOAEL = 13-19 LOAEL = 43-64**
***p*-Dodecylphenol (CASRN 210555-94-5)**	**2100**	No Data > 2000 (RA)	No Data NOAEL = 13-19 LOAEL = 43-65 (RA)	No Data NOAEL = 13-19 LOAEL = 43-64 (RA)	No Data NOAEL = 75 LOAEL = 150 (RA)	No Data NOAEL = 13-19 LOAEL = 43-64 (RA)

Table 4. Summary Table of the Screening Information Data Set as Submitted under the U.S. Challenge Program: Summary of Human Health Data for Aklylphenols Category

Chemical	Acute Oral Toxicity LD_{50} (mg/kg-bw)	Acute Dermal Toxicity LD_{50} (mg/kg-bw)	Repeated-Dose Toxicity NOAEL/LOAEL (mg/kg-bw/day)	Reproductive Toxicity NOAEL/LOAEL (mg/kg-bw/day)	Developmental Toxicity NOAEL/LOAEL (mg/kg-bw/day) Maternal toxicity	Developmental Toxicity NOAEL/LOAEL (mg/kg-bw/day) Developmental toxicity
2,4-Di-*tert*-butylphenol (CASRN 96-76-4)	**1500**	No Data > 1000 (RA)	No Data NOAEL = 100 LOAEL = 600 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)
2,6-Di-*tert*-butylphenol (CAS 128-39-2)	**> 5000**	**> 1000**	**NOAEL = 100 LOAEL = 600**	**NOAEL = 750 LOAEL = NE**	**NOAEL = 150 LOAEL = 750**	**NOAEL = 150 LOAEL = 750**
2,4-Di-*tert*-pentylphenol (CASRN 120-95-6)	**920**	No Data > 1000 (RA)	No Data NOAEL = 100 LOAEL = 600 (RA)	No Data NOAEL = 750 LOAEL = NE (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)
2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CASRN 2772-45-4)	No Data (RA)	No Data > 1000 (RA)	No Data NOAEL = 100 LOAEL = 600 (RA)	No Data NOAEL = 750 LOAEL = NE (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)
2,3,6-Trimethylphenol (CASRN 2416-94-6)	**>2000**	No Data > 1000 (RA)	No Data NOAEL ~ 5 LOAEL ~ 15 (RA)	No Data NOAEL = 750 LOAEL = NE (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)
4-*sec*-Butyl-2,6-tert-butylphenol (CASRN 17540-75-9)	**4800**	No Data > 1000 (RA)	No Data NOAEL ~ 5 LOAEL ~ 15 (RA)	No Data NOAEL = 750 LOAEL = NE (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)
2,4,6-Tri-*tert*-butylphenol (CASRN 732-26-3)	**1670 1610**	No Data > 1000 (RA)	**NOAEL ~ 5 LOAEL ~ 15**	No Data NOAEL = 750 LOAEL = NE (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)

Table 4. Summary Table of the Screening Information Data Set as Submitted under the U.S. Challenge Program : Summary of Human Health Data for Alkylphenols Category (Continued)

Chemical	Mutagenicity – Gene Mutation *In vitro*	Mutagenicity – Chromosomal Aberrations *In vitro*	Mutagenicity – Other Effects: Mouse Micronucleus (*in vivo*)	Irritation (skin)	Irritation (eye)	Carcinogenicity
***o*-Substituted Alkylphenols**						
***o*-*sec*-Butylphenol (CASRN 89-72-5)**	**Negative**	No Data Negative (RA)	—	Corrosive	—	—
2-*tert*-Butylphenol (CASRN 88-18-6)	**Negative**	No Data Negative (RA)	—	Highly irritating	—	—
***p*-Substituted Alkylphenols**						
***p*-*tert*-Butylphenol (CASRN 98-54-4)**	**Negative**	**Negative**	—	Highly irritating or corrosive	—	—
***p*-*sec*-Butylphenol (CASRN 99-71-8)**	**Negative**	**Negative**	—	Corrosive	—	—
***p*-*tert*-Amylphenol (CASRN 80-46-6)**	**Negative**	No Data Negative (RA)	—	Corrosive	—	—
Heptyl derivatives (*p*-heptylphenol) (CASRN 72624-02-3)	**Negative**	No Data Negative (RA)	—	Highly irritating	Highly irritating	—
***p*-*tert*-Octylphenol (CASRN 140-66-9)**	**Negative**	No Data Negative (RA)	—	Mild irritant	Highly irritating	—
***p*-Octylphenol (CASRN 1806-26-4)**	No Data Negative (RA)	No Data Negative (RA)	—	—	—	—
***p*-(alpha, alpha Dimethylbenzyl)-phenol or *p*-cumylphenol (CASRN 599-64-4)**	**Negative**	No Data Negative (RA)	—	—	—	—

Table 4. Summary Table of the Screening Information Data Set as Submitted under the U.S. Challenge Program : Summary of Human Health Data for Alkylphenols Category (Continued)

Chemical	Mutagenicity – Gene Mutation *In vitro*	Mutagenicity – Chromosomal Aberrations *In vitro*	Mutagenicity – Other Effects: Mouse Micronucleus (*in vivo*)	Irritation (skin)	Irritation (eye)	Carcinogenicity
***p*-Nonylphenol (CASRN 84852-15-3)**	**Negative**	**Negative**	**Negative**	Highly irritating or corrosive	Highly irritating or corrosive	—
***p*-Dodecylphenol (CASRN 210555-94-5)**	No Data Negative (RA)	No Data Negative (RA)	—	—	—	—
Di- and Tri-Substituted Mixed Alkylphenols						
2,3,6-Trimethylphenol (CASRN 2416-94-6)	**Negative**	No Data Negative (RA)	—	—	—	—
2,4-Di-*tert*-butylphenol (CASRN 96-76-4)	No Data Negative (RA)	No Data Negative (RA)	—	Moderate irritant	—	—
2,6-Di-*tert*-butylphenol (CAS 128-39-2)	**Negative**	**Negative**	—	Moderate irritant	—	—
2,4-Di-*tert*-pentylphenol (CASRN 120-95-6)	No Data Negative (RA)	No Data Negative (RA)	—	—	—	—
4-*sec*-Butyl-2,6-tert-butylphenol (CASRN 17540-75-9)	**Negative**	**Negative**	—	—	—	—
2,4,6-Tri-*tert*-butylphenol (CASRN 732-26-3)	No Data Negative (RA)	No Data Negative (RA)	—	—	—	**Negative**
2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CASRN 2772-45-4)	No Data Negative (RA)	No Data Negative (RA)	—	Mild irritant	—	—

4 Hazards to the Environment

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 5. The table also indicates where data for tested category members are read-across (RA) to untested members of the category. EPA used a more recent version of ECOSAR, the values in the table may differ from the values submitted in the robust summaries.

Acute Toxicity to Fish

o-Substituted Alkylphenols

o-sec-Butylphenol (CASRN 89-72-5)
A standard acute toxicity test for fish was not provided for *o-sec*-butylphenol. A 96-hour LC_{50} for fish, estimated by ECOSAR (version 1.00), was provided to support evaluation of the acute toxicity.
96-h LC_{50} = 2.6 mg/L (estimated)

2-tert-Butylphenol (CASRN 88-18-6)
(1) Fathead minnow (*Pimephales promelas*) were exposed to an unspecified mixture containing 2.27% 2-*tert*-butylphenol at concentrations of 0, 1, 10, 100 and 1000 mg/L (equivalent to 0, 0.023, 0.23, 2.3 and 23 mg/L 2-*tert*-butylphenol) under static conditions for 96 hours. All affected fish exposed to 1000 mg/L were lethargic, gasping, exhibited erratic swimming and/or were dark in color.
96-h LC_{50} = 15.5 mg/L (680 mg/L of mixture containing 2.27% 2-*tert*-butylphenol)

(2) Due to uncertainty regarding the mixture study above, a 96-hour LC_{50} for fish, estimated by ECOSAR (version 1.00), was provided to give more accurate evaluation of the acute toxicity.
96-h LC_{50} = 2.5 mg/L (estimated)

p-Substituted Alkylphenols

p-tert-Butylphenol (CASRN 98-54-4)
(1) Fathead minnows (*P. promelas*) were exposed to *p-tert*-butylphenol (concentrations not provided) under flow-through conditions for 96 hours with analytical monitoring (no details available).
96-h LC_{50} = 5.14 mg/L

(2) Medaka (*Oryzias latipes*) were exposed to *p-tert*-butylphenol at concentrations of 2.0, 3.0, 4.5, 6.8 and 10 mg/L under semi-static conditions for 96 hours with analytical monitoring (no details available). 100mg/L DMSO and HCO-40 (4:1 weight ratio) was used as a solubliliser. 100 mg/L solubiliser and dechlorinated tap water were used as a control.
96-h LC_{50} = 5.1 mg/L

(3) Fathead minnows (*P. promelas*) were exposed to *p-tert*-butylphenol (concentrations not provided) under flow-through conditions for 96 hours.
96-h LC_{50} = 5.1 mg/L
p-sec-Butylphenol (CASRN 99-71-8)

Juvenile Atlantic salmon (*Salmo salar;*3/concentration) were exposed to *p-sec*-butylphenol at six concentrations (details not provided) under static conditions for 96 hours.
96-h LC_{50} = 0.74 mg/L

p-tert-Amylphenol (CASRN 80-46-6)
A standard acute toxicity test for fish was not provided for *p-tert*-amylphenol. A 96-hour EC_{50} for fish, estimated by ECOSAR (version 1.00), was provided to support the RA evaluation of acute toxicity of *p-tert*-amylphenol.
96-h EC_{50} = 0.8 mg/L (estimated)

p-Heptylphenol (CASRN 72624-02-3)
Groups of rainbow trout (*Oncorhynchus mykiss;*10/concentration) were exposed to *p*-heptylphenol at nominal concentrations of 0.1, 0.35, 3.32, 33.01 and 330.0 mg/L under static conditions for 96 hours.
96-h LC_{50} = 0.85 mg/L

p-tert-Octylphenol (CASRN 140-66-9)
(1) Groups of fathead minnow (*P. promelas*) were exposed to *p-tert*-octylphenol at nominal concentrations of 0.047, 0.091, 0.18, 0.39 and 0.70 mg/L (0.041, 0.077, 0.15, 0.34 and 0.63 mg/L, mean measured concentrations) under flow-through conditions for 96 hours. Mortality, surfacing, loss of equilibrium, dark discoloration and quiescence were observed at the three highest concentrations.
96-h LC_{50} = 0.25 mg/L

(2) In a 60-day fish post-hatch early life-stage test, rainbow trout (*Salmo gairdneri= Oncorhynchus mykiss*) eggs were exposed to *p-tert*-octylphenol at nominal concentrations of 0.0062, 0.012, 0.025, 0.050 and 0.10 mg/L (0.0061, 0.011, 0.022, 0.051 and 0.091 mg/L, mean measured) under flow-through conditions.
60-d NOEC = 0.0061 mg/L
60-d LOEC = 0.011 mg/L

p-Octylphenol (CASRN 1806-26-4)
A standard acute toxicity test for fish was not provided for *p*-octylphenol. A 96-hour EC_{50} for fish, estimated by ECOSAR (version 1.00), was provided to support the RA evaluation of acute toxicity of *p*-octylphenol.
96-h EC_{50} = 0.1 mg/L (estimated)

p-(alpha, alpha-Dimethylbenzyl) phenol (CASRN 599-64-4)
A standard acute toxicity test for fish was not provided for *p*-(alpha, alpha-dimethylbenzyl) phenol. A 96-hour EC_{50} for fish, estimated by ECOSAR (version 1.00), was provided to support the RA evaluation of acute toxicity of *p*-(alpha, alpha-dimethylbenzyl) phenol.
96-h EC_{50} = 0.9 mg/L (estimated)

p-Nonylphenol (CASRN 84852-15-3)
(1) Sheepshead minnows (*Cyprinodon variegatus*) were exposed to *p*-nonylphenol at nominal concentrations of 0.075, 0.125, 0.19, 0.31 and 0.5 mg/L under flow-through conditions for 96 hours. Mean measured concentrations were used for calculations.
96-h LC_{50} = 0.31 mg/L

(2) Fathead minnows (*P. promelas*) were exposed to *p*-nonylphenol under flow-through conditions for 96 hours (test concentrations not provided) with analytical monitoring (details not available). Mean measured concentrations were used for calculations.
96-h LC_{50} =0.128 mg/L

(3) A 33-day chronic toxicity study with *p*-nonylphenol was conducted with fathead minnows (*P. promelas*) at nominal concentrations of 0.003, 0.006, 0.009, 0.015 and 0.025 mg/L under flow-through conditions.
33-d NOEC = 0.0074 mg/L
33-d LOEC = 0.014 mg/L

(4) In another chronic toxicity study, fathead minnows (*P. promelas*) were exposed to *p*-nonylphenol (concentrations not provided) for 28 days with analytical monitoring (details not available).
28-d NOEC = 0.0775 mg/L
28-d LOEC = 0.193 mg/L

p-Dodecylphenol (CASRN 210555-94-5)
(1) Golden orfe (*Leuciscus idus*) were exposed to *p*-dodecylphenol for 96 hours at up to 0.5 mg/L. No effect on mortality was seen.
96-h NOEC = 0.5 mg/L

(2) Atlantic salmon (*S. salar*) were exposed to *p*-dodecylphenol (concentrations not provided) under static conditions for 96 hours.
96-h LC_{50} = 0.14 mg/L

(3) A 96-hour EC_{50} for fish, estimated by ECOSAR (version 1.00), was provided to support the evaluation of acute toxicity of *p*-dodecylphenol.
96-h EC_{50} = 0.01 mg/L (estimated)

Di- and Tri-Substituted Mixed Alkylphenols

2,3,6-Trimethylphenol (CASRN 2416-94-6)
(1) Golden orfe (*L. idus*) were exposed to 2,3,6-trimethylphenol (concentrations not provided) under static conditions for 96 hours.
96-h LC_{50} = 10 - 22 mg/L (geometric mean = 14.8 mg/L)

2,4-Di-tert-butylphenol (CASRN 96-76-4)
(1) Golden orfe (*L. idus*) were exposed to 2,4-di-*tert*-butylphenol for 48 hours.
48-h LC_{50} = 1.8 mg/L

(2) A standard acute toxicity test for fish was not provided for 2,4-di-*tert*-butylphenol. A 96-hour EC_{50} for fish, estimated by ECOSAR (version 1.00), was provided to support the evaluation of acute toxicity of 2,4-di-*tert*-butylphenol.
96-h EC_{50} = 0.1 mg/L (estimated)

2,6-Di-tert-butylphenol (CASRN 128-39-2)
(1) Fathead minnow (*P. promelas*) were exposed to 2,6-di-*tert*-butylphenol at concentrations of 1.0 – 1.4 mg/L under flow-through conditions for 4 - 14 days. Acetone was used as a solvent in this study.
96-h LC_{50} = 1.4 mg/L
14-d LC_{50} = 1.0 mg/L

(2) Zebrafish (*Brachydanio rerio*) were exposed to 2,6-di-*tert*-butylphenol at nominal concentrations of 1.0, 1.8, 3.2, 5.8, 10 and 18 mg/L for 96 hours.
96-h LC_{50} = 7.6 mg/L

(3) Zebrafish (*B. rerio*) were exposed to 2,6-di-*tert*-butylphenol at nominal concentrations of 10 - 24 mg/L under static conditions for 24 - 96 hours. Acetone was used as a solvent in this study.
96-h LC_{50} = 10 mg/L

(4) Rainbow trout (*O. mykiss*) were exposed to 2,6-di-*tert*-butylphenol at mean measured concentrations of 0, 0.21, 0.28, 0.43, 0.66 and 1.0 mg/L under flow-through conditions for 14 days. Acetone was used as a solvent in this study.
96-h LC_{50} > 0.1 mg/L
14-d LC_{50} = 0.74 mg/L

(5) In another study, rainbow trout (*O. mykiss*) were exposed to 2,6-di-*tert*-butylphenol at 0.74 – 1.0 mg/L for 14 days.
96-h LC_{50} > 0.1 mg/L
14-d LC_{50} = 0.74 mg/L

2,4-Di-tert-pentylphenol (CASRN 120-95-6)
A standard acute toxicity test for fish was not provided for 2,4-di-*tert*-pentylphenol. A 96-hour EC_{50} for fish, estimated by ECOSAR (version 1.00), was provided to evaluate the acute toxicity of 2,4-di-*tert*-pentylphenol.
96-h EC_{50} = 0.02 mg/L (estimated)

4-sec-Butyl-2,6-tert-butylphenol (CASRN 17540-75-9)
A standard acute toxicity test for fish was not provided for 4-*sec*-butyl-2,6-*tert*-butylphenol. A 96-hour EC_{50} for fish, estimated by ECOSAR (version 1.00), was provided to evaluate the acute toxicity of 4-*sec*-butyl-2,6-*tert*-butylphenol.
96-h EC_{50} = 0.02 mg/L (estimated)

2,4,6-Tri-tert-butylphenol (CASRN 732-26-3)
A standard acute toxicity test for fish was not provided for 2,4,6-tri-*tert*-butylphenol. A 96-hour EC_{50} for fish, estimated by ECOSAR (version 1.00), was provided to evaluate the acute toxicity of 2,4,6-tri-*tert*-butylphenol.
96-h EC_{50} = 0.04 mg/L (estimated)

2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CASRN 2772-45-4)
A standard acute toxicity test for fish was not provided for 2,4-bis(alpha, alpha-dimethylbenzyl)phenol. A 96-hour EC_{50} for fish, estimated by ECOSAR (version 1.00), was provided to evaluate the acute toxicity of 2,4-bis(alpha, alpha-dimethylbenzyl) phenol.
96-h EC_{50} = 0.02 mg/L (estimated)

Acute Toxicity to Aquatic Invertebrates

o-Substituted Alkylphenols

o-sec-Butylphenol (CASRN 89-72-5)
(1) *Crangon septemspinosa* (shrimp) were exposed to *o-sec*-butylphenol for 96 hours; test conditions were not provided.
96-h LC_{50} = 1.3 mg/L

(2) A standard acute toxicity test for aquatic invertebrates was not provided for *o-sec*-butylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the acute toxicity of *o-sec*-butylphenol.
48-h EC_{50} = 1.5 mg/L (estimated)

2-tert-Butylphenol (CASRN 88-18-6)
(1) *C. septemspinosa* (shrimp) were exposed to *o-sec*-butylphenol for 96 hours; test conditions were not provided.
96-h LC_{50} = 2.4 mg/L

(2) A standard acute toxicity test for aquatic invertebrates was not provided for 2-*tert*-butylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to support the RA evaluation of acute toxicity of 2-*tert*-butylphenol.
48-h EC_{50} = 1.4 mg/L (estimated)

p-Substituted Alkylphenols

p-tert-Butylphenol (CASRN 98-54-4)
(1) *D. magna* were exposed to *p-tert*-butylphenol for 48 hours; test conditions were not provided.
48-h EC_{50} = 3.9 mg/L

(2) *Daphnia magna* (4 replicates;5 organisms/replicate) were exposed to *p-tert*-butylphenol at nominal concentrations of 1.0, 1.8 3.2, 5.6 and 10.0 mg/L under semi-static conditions for 48 hours. 10 mg/LDMSO and HCO-40 (4:1 weight ratio) was used as a solubiliser. 10 mg/L solubiliser and dechlorinated tap water were used as a control.
48-h EC_{50} = 6.7 mg/L

(3) *D. magna* were exposed to 3 - 4 unspecified concentrations of *p-tert*-butylphenol under static conditions for 48 hours.
48-h EC_{50} = 3.4 mg/L

(4) *D. magna* were exposed to *p-tert*-butylphenol at nominal concentrations of 0.073, 0.23, 0.73, 2.3 and 7.3 mg/L under semi-static conditions for 21 days. DMSO and HCO-40 (4:1 mixture, 7.3 mg/L) was added as a solubiliser. Mean measured concentrations were 0.037, 0.062, 0.12, 0.26 and 0.51 mg/L.
21-d reproduction EC_{50} = 2.0 mg/L
21-d LOEC = 7.3 mg/L
21-d NOEC = 2.3 mg/L

(5) *C. septemspinosa* (shrimp) were exposed to *p-tert*-butylphenol for 96 hours; test conditions were not provided.
96-h LC_{50} = 1.9 mg/L

p-sec-Butylphenol (CASRN 99-71-8)
(1) *Daphnia magna* (10/ beaker) were exposed to *p-sec*-butylphenol under semi-static conditions for 96 hours.
96-h NOEC = 58.5- 64.3 µM

(2) *C. septemspinosa* (shrimp; 4/concentration) were exposed to *p-sec*-butylphenol under static conditions for 96 hours.
96-h LC_{50} = 1.8 mg/L

(3) A standard acute toxicity test for aquatic invertebrates was not provided for *p-sec*-butylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to support the evaluation of acute toxicity of *p-sec*-butylphenol.
48-h EC_{50} = 1.9 mg/L (estimated)

p-tert-Amylphenol (CASRN 80-46-6)
(1) *C. septemspinosa* (shrimp) were exposed to *p-tert*-amylphenol for 96 hours; test conditions were not provided.
96-h LC_{50} = 1.7 mg/L

(2) A standard acute toxicity test for aquatic invertebrates was not provided for *p-tert*-amylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to give more accurate evaluation of acute toxicity of *p-tert*-amylphenol.
48-h EC_{50} = 0.8 mg/L (estimated)

Heptyl derivatives (p-heptylphenol) (CASRN 72624-02-3)
(1) A standard acute toxicity test for aquatic invertebrates was not provided for *p*-heptylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to support the RA evaluation of acute toxicity of *p*-heptylphenol.
48-h EC_{50} = 0.4 mg/L (estimated)

(2) A standard chronic toxicity test for aquatic invertebrates was not provided for *p*-heptylphenol. A 21 -day chronic value for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the chronic toxicity of *p*-heptylphenol.
21-d ChV = 0.07 mg/L (estimated)

p-tert-Octylphenol (CASRN 140-66-9)
(1) *D. magna* were exposed to *p-tert*-octylphenol under flow-through conditions for 48 hours. Mean measured concentrations were 0.063, 0.11, 0.19, 0.32 and 0.94 mg/L.
48-h LC_{50} = 0.27 mg/L
48-h NOEC = 0.11 mg/L

(2) *D. magna* were exposed to *p-tert*-octylphenol under flow-through conditions for 21 days. Mean measured concentrations were 0.037, 0.062, 0.12, 0.23 and 0.51 mg/L.
21-d EC_{50} = 0.34 mg/L
21-d NOEC = 0.037 mg/L

(3) *Gammarus pulex (freshwater shrimp)* were exposed to *p-tert*-octylphenol for 96 hours under semi-static conditions.
96-h EC_{50} = 0.013 mg/L
96-h LC_{50} = 0.019 mg/L

p-Octylphenol (CASRN 1806-26-4)
(1) A standard acute toxicity test for aquatic invertebrates was not provided for *p*-octylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to support the RA evaluation of acute toxicity of *p*-octylphenol.
48-h EC_{50} = 0.1 mg/L (estimated)

(2) A standard chronic toxicity test for aquatic invertebrates was not provided for *p*-octylphenol. A 21 -day chronic value for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to support the RA evaluation of chronic toxicity of *p*-octylphenol.
21-d ChV = 0.02 mg/L (estimated)

p-(alpha, alpha-Dimethylbenzyl)phenol (CASRN 599-64-4)
(1) A standard acute toxicity test for aquatic invertebrates was not provided for *p*-cumylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to support the RA evaluation of acute toxicity of *p*-cumylphenol.
48-h EC_{50} = 0.7 mg/L (estimated)

(2) A standard chronic toxicity test for aquatic invertebrates was not provided for *p*-cumylphenol. A 21-day chronic value for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to support the RA evaluation of chronic toxicity of *p*-cumylphenol.
21-d ChV = 0.13 mg/L (estimated)

p-Nonylphenol (CASRN 84852-15-3)
(1) *D. magna* were exposed to *p*-nonylphenol for 48-hours; test conditions were not provided. A solvent (acetone) was used in the test, but no solvent control was reported.
48-h EC_{50} = 0.14 mg/L

(2) *D. magna* were exposed to *p*-nonylphenol for 48 hours; test conditions were not provided.
48-h EC_{50} = 0.085 mg/L

(3) Mysid shrimp (*Mysidopsis bahia)* were exposed to *p*-nonylphenol under flow-through conditions for 96 hours.
96-h LC_{50} = 0.043 mg/L
96-h NOEC = 0.018 mg/L

(4) In a 21-day reproduction test, *D. magna* were exposed to *p*-nonylphenol under semi-static conditions.
48-h LC_{50} = 0.19 mg/L
21-d LC_{50} = 0.10 mg/L
21-d NOEC (offspring survival) = 0.024 mg/L
21-d NOEC (length) = 0.039 mg/L

(5) Mysid shrimp (*M. bahia)* were exposed to p-nonylphenol under static conditions for 28 days.
28-d LOEC (length) = 0.0067 mg/L
28-d NOEC (length) = 0.0039 mg/L

p-Dodecylphenol (CASRN 210555-94-5)
(1) *Daphnia magna* were exposed to *p*-dodecylphenol under static conditions for 48 hours. Measured concentrations were used for calculations.
48-h EC_{50} = 0.093 mg/L

(2) Sand shrimp (*Crangon septemspinosa*) were exposed to *p*-dodecylphenol under semi-static conditions for 96 hours.
96-h EC_{50} = 0.15 mg/L

(3) A standard chronic toxicity test for aquatic invertebrates was not provided for *p*-dodecylphenol. A 21-day chronic value for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to support the RA evaluation of chronic toxicity of *p*-dodecylphenol.
21-d ChV = 0.003 mg/L (estimated)

Di- and Tri-Substituted Mixed Alkylphenols

2,3,6-Trimethylphenol(CASRN 2416-94-6)
(1) *D. magna* were exposed to 2,3,6-trimethylphenol for 24 hours; test conditions were not reported.
24-h EC_{50} = 12.6 mg/L

(2) *D. magna* were exposed to 2,3,6-trimethylphenol at nominal concentrations of 0.1, 0.35, 1, 3.5, 10, 35, 100, 350 mg/L under static conditions for 24 hours.
24-h EC_{50} = 19.5 mg/L

(3) A standard acute toxicity test for aquatic invertebrates was not provided for 2,3,6-trimethylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to give more accurate evaluation of acute toxicity of 2,3,6-trimethylphenol.
48-h EC_{50} = 2.8 mg/L (estimated)

2,4-Di-tert-butylphenol (CASRN 96-76-4)
(1) A standard acute toxicity test for aquatic invertebrates was not provided for 2,4-di-tert-butylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the acute toxicity of 2,4-di-tert-butylphenol.
48-h EC_{50} = 0.2 mg/L (estimated)

(2) A standard chronic toxicity test for aquatic invertebrates was not provided for 2,4-di-tert-butylphenol. A 21-day chronic value for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the chronic toxicity of 2,4-di-tert-butylphenol.
21-d ChV = 0.03 mg/L (estimated)

2,6-Di-tert-butylphenol (CASRN 128-39-2)
(1) *D. magna* were exposed to 2,6-di-tert-butylphenol under static conditions for 24 hours. Nominal concentrations were, 0.58, 1.0, 1.8, 3.2 and 5.3 mg/L.
24-h EC_{50} = 1.7 mg/L

(2) *D. magna* were exposed to 2,6-di-tert-butylphenol under static conditions for 24 hours. Nominal concentrations were, 0.32, 0.58, 1.0, 1.8, 3.2, 5.8, 10.0 and 18.0 mg/L.
24-h EC_{50} = 5.5 mg/L

(3) *D. magna* were exposed to 2,6-di-tert-butylphenol under flow-through conditions for 48 hours.
48-h EC_{50} = 0.45 mg/L
48-h NOEC = 0.076 mg/L

(4) Scud (*Gammarus fasciatus)* were exposed to 2,6-di-*tert*-butylphenol under flow-through conditions for 96 hours. Acetone was used as a solvent.
48-h LC_{50} = 0.80 mg/L
72-h LC_{50} = 0.70 mg/L
96-h LC_{50} = 0.60 mg/L
96-h NOEC = 0.38 mg/L

(5) A standard chronic toxicity test for aquatic invertebrates was not provided for 2,6-di-tert-butylphenol. A 21-day chronic value for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the chronic toxicity of 2,6-di-tert-butylphenol.
21-d ChV = 0.08 mg/L (estimated)

2,4-Di-tert-pentylphenol (CASRN 120-95-6)
(1) A standard acute toxicity test for aquatic invertebrates was not provided for 2,4-di-*tert*-pentylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the acute toxicity of 2,4-di-*tert*-pentylphenol.
48-h EC_{50} = 0.04 mg/L (estimated)

(2) A standard chronic toxicity test for aquatic invertebrates was not provided for 2,4-di-*tert*-pentylphenol. A 21-day chronic value for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the chronic toxicity of 2,4-di-*tert*-pentylphenol.
21-d ChV = 0.008 mg/L (estimated)

4-sec-Butyl-2,6-tert-butylphenol (CASRN 17540-75-9)
(1) A standard acute toxicity test for aquatic invertebrates was not provided for 4-*sec*-butyl-2,6-tert-butylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the acute toxicity.
48-h EC_{50} = 0.04 mg/L (estimated)

(2) A standard chronic toxicity test for aquatic invertebrates was not provided for 4-*sec*-butyl-2,6-tert-butylphenol. A 21-day chronic value for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the chronic toxicity of 4-*sec*-butyl-2,6-tert-butylphenol.
21-d ChV = 0.008 mg/L (estimated)

2,4,6-Tri-tert-butylphenol (CASRN 732-26-3)
(1) A standard acute toxicity test for aquatic invertebrates was not provided for 2,4,6-tri-*tert*-butylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the acute toxicity of 2,4,6-tri-*tert*-butylphenol.
48-h EC_{50} = 0.07 mg/L (estimated)

(2) A standard chronic toxicity test for aquatic invertebrates was not provided for 2,4,6-tri-*tert*-butylphenol. A 21-day chronic value for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the chronic toxicity of 2,4,6-tri-*tert*-butylphenol.
21-d ChV = 0.013 mg/L (estimated)

2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CASRN 2772-45-4)
(1) A standard acute toxicity test for aquatic invertebrates was not provided for 2,4-bis(alpha, alpha-dimethylbenzyl)phenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the acute toxicity of 2,4-bis(alpha, alpha-dimethylbenzyl) phenol.
48-h EC_{50} = 0.04 mg/L (estimated)

(2) A standard chronic toxicity test for aquatic invertebrates was not provided for 2,4-bis(alpha, alpha-dimethylbenzyl)phenol. A 21-day chronic value for *Daphnia*, estimated by ECOSAR (version 1.00), was provided to evaluate the chronic toxicity of 2,4-bis(alpha, alpha-dimethylbenzyl)phenol.
21-d ChV = 0.007 mg/L (estimated)

Toxicity to Aquatic Plants

o-Substituted Alkylphenols

o-sec-Butylphenol (CASRN 89-72-5)
A standard acute toxicity test for aquatic plants was not provided for *o-sec*-butylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the aquatic plant toxicity of *o-sec*-butylphenol.
96-h EC_{50} = 6.1 mg/L (estimated)

2-tert-Butylphenol (CASRN 88-18-6)
A standard toxicity test for aquatic plants was not provided for 2-*tert*-butylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the aquatic plant toxicity of 2-*tert*-butylphenol.
96-h EC_{50} = 5.8 mg/L (estimated)

p-Substituted Alkylphenols

p-tert-Butylphenol (CASRN 98-54-4)
(1) Green algae (*Selenastrum capricornutum (*new name: *Pseudokirchneriella subcapitata*)) were exposed to *p-tert*-butylphenol at nominal concentrations of 9.53, 17.2, 30.9, 55.6 and 100mg/L under static (open-system) conditions for 72 hours. Minimal amount of tween 80 – acetone (1:1) or DMSO-HCO 40 (9:1) was used as a stabilizer.
72-h EC_{50} (biomass) = 22.7 mg/L
72-h NOEC (biomass) = 9.53 mg/L

p-sec-Butylphenol (CASRN 99-71-8)
A standard toxicity test for aquatic plants was not provided for *p-sec*-butylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the aquatic plant toxicity of *p-sec*-butylphenol.
96-h EC_{50} = 7.9 mg/L (estimated)

p-tert-Amylphenol (CASRN 80-46-6)
A standard toxicity test for aquatic plants was not provided for *p-tert*-amylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the aquatic plant toxicity of *p-tert*-amylphenol.
96-h EC_{50} = 2.3 mg/L (estimated)

Heptyl derives (p-heptylphenol) (CASRN 72624-02-3)
(1) Green algae (*S. capricornutum (*new name: *P. subcapitata*) were exposed to *p*-heptylphenol at nominal concentrations of 0.3, 3.3, 33, 330 and 3300 mg/L under static conditions for 96 hours.
96-h EC_{50} (biomass) = 0.83 mg/L
96-h EC_{50} (growth rate) = 2.5 mg/L

p-tert-Octylphenol (CASRN 140-66-9)
(1) Green algae (*S. capricornutum (*new name: *P. subcapitata*)) were exposed to *p-tert*-octylphenol under static conditions for 96 hours. Nominal concentrations were 1.0, 1.8, 3.2, 5.6 and 10.0 mg/L.
96-h EC_{50} (biomass) = 1.9 mg/L
96-h NOEC < 1.0 mg/L

(2) Green algae (*Scenedesmus subspicatus*) were exposed to *p-tert*-octylphenol under static conditions for 72 hours.
72-h EC_{50} = 1.1 mg/L

p-Octylphenol (CASRN 1806-26-4)
A standard toxicity test for aquatic plants was not provided for *p*-octylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR, was provided to evaluate the aquatic plant toxicity of *p*-octylphenol.
96-h EC_{50} = 0.4 mg/L (estimated)

p-(alpha, alpha-Dimethylbenzyl)phenol (CASRN 599-64-4)
A standard toxicity test for aquatic plants was not provided for *p*-cumylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the aquatic plant toxicity of *p*-cumylphenol.
96-h EC_{50} = 2.6 mg/L (estimated)

p-Nonylphenol (CASRN 84852-15-3)
(1) Green algae (*S. capricornutum (*new name: *P. subcapitata*)) were exposed to *p*-nonylphenol under static conditions for 96 hours. Robust summary reports analytical monitoring was conducted; however, reports nominal concentrations as 0.06, 0.12, 0.25 and 0.5 mg/L. Mean measured concentrations were used for calculations.
96-h EC_{50} (biomass) = 0.41 mg/L

(2) Green algae (*S. subspicatus*) were exposed to *p*-nonylphenol for 72 hours, test conditions were not provided.
72-h EC_{50} (biomass) = 0.0563 mg/L

(3) Marine alga, diatom (*Skeletonema costatum)* was exposed to *p*-nonylphenol under static conditions for 96 hours. Robust summary reports analytical monitoring was conducted, but details were not provided.
96-h EC_{50} (growth) = 0.027 mg/L

p-Dodecylphenol (CASRN 210555-94-5)
(1) Green algae (*S. subspicatus)* were exposed to *p*-dodecylphenol under static conditions for 72 hours.
72-h EC_{50} (biomass) = 0.77 mg/L
72-h EC_{50} (growth) = 0.77 mg/L

(2) A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the aquatic plant toxicity of *p*-dodecylphenol.
96-h EC_{50} = 0.05 mg/L (estimated)

Di- and Tri-Substituted Mixed Alkylphenols

2,3,6-Trimethylphenol (CASRN 2416-94-6)
(1) Green algae (*S. subspicatus*) were exposed to 2,3,6-trimethylphenol under conditions for 72 hours; test conditions were not provided.
72-h EC_{50} = 19.0 mg/L

(2) A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the aquatic plant toxicity of 2,3,6-trimethylphenol.
96-h EC_{50} = 11.9 mg/L (estimated)

2,4-Di-tert-butylphenol (CASRN 96-76-4)
A standard toxicity test for aquatic plants was not provided for 2,4-di-*tert*-butylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the aquatic plant toxicity of 2,4-di-*tert*-butylphenol.
96-h EC_{50} = 0.6 mg/L (estimated)

2,6-Di- tert-butylphenol (CASRN 128-39-2)
(1) Green algae (*S. capricornutum (*new name: *P. subcapitata*)) were exposed to 2,6-*di-tert*-butylphenol under static conditions for 96 hours. Mean measured concentrations were 0.11, 0.24, 0.51, 1.23 and 2.17 mg/L. Acetone was used as a solvent in the study.
72-h EC_{50} (biomass) = 0.51 mg/L
96-h EC_{50} (biomass) = 0.56 mg/L

(2) Green algae (*S. capricornutum (*new name: *P. subcapitata*)) were exposed to 2,6-di-*tert*-butylphenol under static conditions for 96 hr. Initial measured concentrations were 7.2, 2.9, 2.1, 1.2, 0.63 and 0.33 mg A.I./L (time-weighted average concentrations were 2.2, 0.95, 0.64, 0.34, 0.18 and 0.086 mg A.I./L). Acetone was used as a solvent in the study.
72-h EC_{50} (biomass) = 1.4 mg A.I./L
96-h EC_{50} (biomass) = 1.2 mg A.I./L
96-h NOEC = 0.64 mg A.I./L

2,4-Di-tert-pentylphenol (CASRN 120-95-6)
A standard toxicity test for aquatic plants was not provided for 2,4-di-*tert*-pentylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the

aquatic plant toxicity of 2,4-di-*tert*-pentylphenol.
96-h EC_{50} = 0.1 mg/L (estimated)

4-sec-Butyl-2,6-tert-butylphenol (CASRN 17540-75-9)
A standard toxicity test for aquatic plants was not provided for 4-*sec-butyl*-2,6-*tert*-butylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the aquatic plant toxicity of 4-*sec*-butyl-2,6-*tert*-butylphenol.
96-h EC_{50} = 0.1 mg/L (estimated)

2,4,6-Tri-tert-butylphenol (CASRN 732-26-3)
A standard toxicity test for aquatic plants was not provided for 2,4,6-tri-*tert*-butylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the aquatic plant toxicity of 2,4,6-tri-*tert*-butylphenol.
96-h EC_{50} = 0.2 mg/L (estimated)

2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CASRN 2772-45-4)
A standard toxicity test for aquatic plants was not provided for 2,4-bis(alpha, alpha-dimethylbenzyl)phenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR (version 1.00), was provided to evaluate the aquatic plant toxicity of 2,4-bis(alpha, alpha-dimethylbenzyl)phenol.
96-h EC_{50} = 0.1 mg/L (estimated)

Conclusion:

o-Substituted Alkylphenols

For acute hazard of *o*-substituted alkylphenols subcategory, the estimated 96-hour LC_{50} to fish is 2.5 mg/L, the measured 48-hour EC_{50} to aquatic invertebrates is 1.3 mg/L, and the estimated 96-hour EC_{50} to aquatic plants is 5.8 mg/L .

Data gaps for acute toxicity to fish and aquatic plants were identified under the HPV Challenge Program for the *o*-substituted alkylphenols subcategory.

p-Substituted Alkylphenols

For acute hazard of *p*-substituted alkylphenols subcategory, the measured 96-hour LC_{50} values to fish range from 0.13 to 5.1 mg/L , the measured 48-hour EC_{50} values to aquatic invertebrates range from 0.09 to 6.7 mg/L, and the measured 72/96-hour EC_{50} values to aquatic plants range from 0.06 to 22.7 mg/L . The measured chronic hazard of *p*-substituted alkylphenols subcategory ranges from 0.024 to 2.3 mg/L for 21-day *Daphnia magna* toxicity.

No data gaps were identified under the HPV Challenge Program for the *p*-substituted alkyphenols subcategory.

Di- and Tri-Substituted Mixed Alkylphenols

For acute hazard of di- and tri-substituted alkylphenols subcategory, the measured/estimated 96-hour LC_{50} values to fish range from 0.02 to 14.8 mg/L , the measured/estimated 48-hour EC_{50} values to aquatic invertebrates range from 0.04 to 2.8 mg/L, and the measured/estimated 72/96-hour EC_{50} values to aquatic plants range from 0.1 to 19 mg/L . The estimated chronic hazard of *p*-substituted alkylphenols subcategory ranges from 0.008 to 0.08 mg/L for 21-day *Daphnia magna* toxicity.

A data gap for chronic toxicity to aquatic invertebrates was identified under the HPV Challenge Program for the di- and tri-substituted mixed alkylphenols subcategory.

Table 5. Summary of Environmental Effects – Aquatic Toxicity Data

Chemical	Acute Toxicity to Fish 96 h-LC_{50} (mg/L)	Acute Toxicity to Aquatic Invertebrates 48-h EC_{50} (mg/L)	Toxicity to Aquatic Plants 96-h EC_{50} (mg/L)	Chronic Toxicity NOEC (mg/L)
***o*-Substituted Alkylphenols**				
***o*-*sec*-Butylphenol (CAS No. 89-72-5)**	2.6 (e)	**1.3(m)** 1.5 (e)	6.1 (e)	—
2-*tert*-Butylphenol (CAS No. 88-18-6)	2.5 (e)	**2.4 (m)** 1.4 (e)	5.8 (e)	—
***p*-Substituted Alkylphenols**				
***p*-*tert*-Butylphenol (CAS No. 98-54-4)**	**5.1 (m)**	**3.4 – 6.7 (m)**	**22.7 (m) (72-h)**	**21-d daphnid = 2.3(m)** —
***p*-*sec*-Butylphenol (CAS No. 99-71-8)**	**0.74 (m)**	**1.8 (m)** (96-h) 1.9 (e)	7.9 (e)	—
***p*-*tert*-Amylphenol (CAS No. 80-46-6)**	0.8 (e)	**1.7 (m)** (96-h) 0.8 (e) (48-h)	2.3 (e)	—
Heptyl derivatives (*p*-heptylphenol) (CAS No. 72624-02-3)	**0.85 (m)**	RA 0.27(m) 0.4 (e)	**0.83 (m)** (biomass) **2.5 (m)** (growth rate)	RA 0.037(m) 0.07(e)
***p*-*tert*-Octylphenol (CAS No. 140-66-9)**	**0.25 (m)**	**0.27 (m)**	**1.9 (m)** (biomass) **1.1 (m)** (72-h)	**60-d fish = 0.0061 (m) 21-d daphnid = 0.037(m)**
***p*-Octylphenol (CAS No. 1806-26-4)**	RA 0.25(m) 0.1 (e)	RA 0.27(m) 0.1 (e)	RA 0.41(m) 0.4 (e)	RA 0.037(m) 0.02(e)
***p*-(alpha, alpha-Dimethylbenzyl)phenol or *p*-cumylphenol (CAS No. 599-64-4)**	RA 0.25(m) 0.9 (e)	RA 0.27(m) 0.7 (e)	RA 1.1(m) 2.6 (e)	RA 0.037(m) 0.13(e)
***p*-Nonylphenol (CAS No. 84852-15-3)**	**0.128 – 0.31 (m)**	**0.085 – 0.19 (m)**	**0.41 (m)** (biomass) **0.0563 (m) (72-h)** (biomass)	**28-d fish = 0.0775 (m) 33-d fish = 0.0074 (m) 21-d daphnid = 0.024-0.039 (m)**
***p*-Dodecylphenol (CAS No. 210555-94-5)**	**0.14 – 0.5 (m)** 0.01 (e)	**0.093 (m)**	**0.77 (m) (72-h)** 0.05 (e)	RA 0.037(m) 0.003(e)
Di- and Tri--Substituted Mixed Alkylphenols				
2,3,6-Trimethylphenol (CAS No. 2416-94-6)	**14.8 (m)**	**12.6 (m) (24-h)** 2.8 (e)	**19 (m) (72-h)** 11.9 (e)	—
2,4-Di-*tert*-butylphenol (CAS No. 96-76-4)	**1.8 (m) (48-h)** 0.1 (e)	0.2 (e)	0.6 (e)	0.03 (e)
2,6-Di-*tert*-butylphenol (CAS No. 128-39-2)	**0.74 – 10 (m)**	**0.45 (m)**	**0.5 – 1.2 (m)** (biomass)	0.08 (e)
2,4-Di-*tert*-pentylphenol	0.02 (e)	0.04 (e)	0.1 (e)	0.008 (e)

Table 5. Summary of Environmental Effects – Aquatic Toxicity Data				
Chemical	**Acute Toxicity to Fish 96 h-LC_{50} (mg/L)**	**Acute Toxicity to Aquatic Invertebrates 48-h EC_{50} (mg/L)**	**Toxicity to Aquatic Plants 96-h EC_{50} (mg/L)**	**Chronic Toxicity NOEC (mg/L)**
(CAS No. 120-95-6)				
4-*sec*-Butyl-2,6-*tert*-butylphenol (CAS No. 17540-75-9)	0.02 (e)	0.04 (e)	0.1 (e)	0.008 (e)
2,4,6-Tri-*tert*-butylphenol (CAS No. 732-26-3)	0.04 (e)	0.07 (e)	0.2 (e)	0.013 (e)
2,4-bis(alpha, alpha)Dimethylbenzyl)-phenol (CAS No. 2772-45-4)	0.02 (e)	0.04 (e)	0.1 (e)	0.007 (e)

(m) = measured data (i.e. derived from testing); (e) = estimated data (i.e., derived from modeling);
RA= read-across

5 References

1. Cunny, H.C., Mayes, B.A., Rosica, K.A., Trutter, J.A., and Van Miller, J.P. (1997) Subchronic toxicity (90- day) study with *para*-nonylphenol in rats. Regulatory Toxicology and Pharmacology 26:172-178.

2. NTP Report # RACB94021. Abstract for Repro Tox: Nonylphenol, branched. Reproductive toxicity of nonylphenol (CASRN 84852-15-3) administered by gavage to sprague-dawley rats.

3. NTIS Technical Report (NTIS/PB97-210900) (NTP-RACB-94-021). (1997) Sep; 572pp. Final Report on the reproductive toxicity of nonylphenol (CASRN 84852-15-3) administered in the diet to sprague-dawley rats.

4. Tyl, R.W., Myers, C.B., Marr, M.C., Brine, D.R., Fail, P.A., Seely, J.C., and Van Miller, J.P. (1999) Two-generation reproduction study with para-tert-octylphenol in rats. Regulatory Toxicology and Pharmacology 30:81-95.