SCREENING-LEVEL HAZARD CHARACTERIZATION FOR HIGH PRODUCTION VOLUME CHEMICALS

CHEMICAL CATEGORY NAME
Alkylphenols

SPONSORED CHEMICALS

***o*-Substituted Alkylphenols (2 chemicals)**
***p*-Substituted alkylphenols (9 chemicals)**
Di- and Tri-Substituted Mixed Alkylphenols (7 chemicals)

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SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

The High Production Volume (HPV) Challenge Program[1] is 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 sponsor chemicals; sponsorship entails the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data do 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]) 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 1,400 sponsored chemicals. OPPT is using a hazard-based screening process to prioritize review of the submissions. The hazard-based screening process consists of two tiers described below briefly and in more detail on the Hazard Characterization website[3].

Tier 1 is a computerized sorting process whereby key elements of a submitted data set are compared to established criteria to "bin" chemicals/categories for OPPT review. This is an automated process performed on the data as submitted by the sponsor. It does not include evaluation of the quality or completeness of the data.

In Tier 2, a screening-level hazard characterization is developed by EPA that consists of an objective evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. The evaluation is performed according to established EPA guidance[2,4] and is based primarily on hazard data provided by sponsors. EPA may also include additional or updated hazard information of which EPA, sponsors or other parties have become aware. The hazard characterization may also identify data gaps that will become the basis for a subsequent data needs assessment where deemed necessary. Under the HPV Challenge Program, chemicals that have similar chemical structures, properties and biological activities may be grouped together and their data shared across the resulting category. This approach often significantly reduces the need for conducting tests for all endpoints for all category members. As part of Tier 2, evaluation of chemical category rationale and composition and data extrapolation(s) among category members is performed in accord with established EPA[2] and OECD[5] guidance.

The screening-level hazard characterizations that emerge from Tier 2 are important contributors to OPPT's existing chemicals review process. These hazard characterizations are technical documents intended to support 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. The public, including sponsors, may offer comments on the hazard characterization documents.

The screening-level hazard characterizations, as the name indicates, do not evaluate the potential risks of a chemical or a chemical category, but will serve as a starting point for such reviews. In 2007, EPA received data on uses of and exposures to high-volume TSCA existing chemicals, submitted in accordance with the requirements of the Inventory Update Reporting (IUR) rule. For the chemicals in the HPV Challenge Program, EPA will review the IUR data to evaluate exposure potential. The resulting exposure information will then be combined with the screening-level hazard characterizations to develop screening-level risk characterizations[4,6]. The screening-level risk characterizations will inform EPA on the need for further work on individual chemicals or categories. Efforts are currently underway to consider how best to utilize these screening-level risk characterizations as part of a risk-based decision-making process on HPV chemicals which applies the results of the successful U.S. High Production Volume Challenge Program and the IUR to support judgments concerning the need, if any, for further action.

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[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.
[3] U.S. EPA. HPV Chemicals Hazard Characterization website (http://www.epa.gov/hpvis/abouthc.html).
[4] U.S. EPA. Risk Assessment Guidelines; http://cfpub.epa.gov/ncea/raf/rafguid.cfm.
[5] OECD. Guidance on the Development and Use of Chemical Categories; http://www.oecd.org/dataoecd/60/47/1947509.pdf.
[6] U.S. EPA. Risk Characterization Program; http://www.epa.gov/osa/spc/2riskchr.htm.

SCREENING-LEVEL HAZARD CHARACTERIZATION
Alkylphenols Category

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 alkylphenols category consists of the following chemicals:

o-Substituted Alkylphenols	
o-sec-Butylphenol	CAS No. 89-72-5
2-*tert*-Butylphenol	CAS No. 88-18-6
p-Substituted Alkylphenols	
p-tert-Butylphenol	CAS No. 98-54-4
p-sec-Butylphenol	CAS No. 99-71-8
p-tert-Amylphenol	CAS No. 80-46-6
Heptyl derivatives (*p*-heptylphenol)	CAS No. 72624-02-3
p-tert-Octylphenol	CAS No. 140-66-9
p-Octylphenol	CAS No. 1806-26-4
p-(alpha, alpha-Dimethylbenzyl)phenol or *p*-cumylphenol	CAS No. 599-64-4
p-Nonylphenol	CAS No. 84852-15-3
p-Dodecylphenol	CAS No. 210555-94-5
Di- and Tri-Substituted Mixed Alkylphenols	
2,3,6-Trimethylphenol	CAS No. 2416-94-6
2,4-Di-*tert*-Butylphenol	CAS No. 96-76-4
2,6-Di- *tert*-Butylphenol	CAS No. 128-39-2
2,4-Di-*tert*-pentylphenol	CAS No. 120-95-6
4-sec-Butyl-2,6-tert-butylphenol	CAS No. 17540-75-9
2,4,6-Tri-*tert*-butylphenol	CAS No. 732-26-3
2,4-Bis(alpha, alpha-dimethylbenzyl)phenol or *o,p*-cumylphenol or 2,4-di-cumylphenol	CAS No. 2772-45-4

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

This screening-level hazard characterization is based primarily on the review of the test plan and robust summaries of studies submitted by the sponsor(s) under the HPV Challenge Program. 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. Structure(s) of the sponsored chemical(s) is included in the appendix. The screening-level hazard characterization for environmental and human health toxicity is based largely on SIDS endpoints and is described according to established EPA or OECD effect level definitions and hazard assessment practices.

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 based on the position and the extent of substitution on the phenols.

Summary-Conclusion

The log K_{ow} of the members of the *o*-substituted alkylphenols subcategory indicates that their potential to bioaccumulate is expected to be low. The log K_{ow} of the members of the *p*-substituted alkylphenols subcategory with the smaller alkyl groups (butyl) indicates that their potential to bioaccumulate is expected to be low; the category members with the larger alkyl substituents have higher log K_{ow} values (mostly above 4) indicating their potential to bioaccumulate is expected to be high. The log K_{ow} of the di- and tri-substituted mixed alkylphenols subcategory members indicates that the potential to bioaccumulate is expected to be high.

o-Substituted alkylphenol subcategory members are not readily biodegradable, indicating that they have the potential to persist in the environment. Of the *p*-substituted alkylphenol subcategory members, *p-tert*-butylphenol and *p-sec*-butylphenol, are readily biodegradable, indicating that they do not have the potential to persist in the environment. All other *p*-substituted alkylphenol subcategory members are not readily biodegradable, indicating that they have the potential to persist in the environment. Di- and tri-substituted mixed alkylphenols subcategory members are not readily biodegradable, indicating that they have the potential to persist in the environment.

The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of *o*-substituted alkylphenols subcategory to aquatic organisms is moderate. The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of the majority of *p*-substituted alkylphenols subcategory to aquatic organisms is moderate. A few of the category members have high aquatic plant toxicity values, indicating that they may pose a high hazard to aquatic plants. The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of di- and tri-substituted mixed alkylphenols subcategory to aquatic organisms is moderate to high. Generally, the hazard potential for the category members with smaller substituents is moderate. Estimated toxicity values for category members with larger substituents indicate high potential hazard for fish and aquatic plants.

The acute oral toxicity for the members the alkylphenols category is low to moderate. Repeated exposures via the oral route of exposure resulted in effects on liver, kidney, testes and forestomach. Two- and three-generation reproduction toxicity studies indicate no treatment-related effects on reproductive or developmental endpoints, except body weight effects, in parents or offspring. No abnormalities in fetuses were reported for any members of the alkylphenol category. None of the category members showed mutagenic potential when tested in *Salmonella typhimurium.* No chromosomal aberrations were observed in cells tested with or without metabolic activation for any of the category members. When tested *in vivo* in a mouse micronucleus assay, *p*-nonylphenol did not induce cytogenetic damage. The category members are considered irritating to corrosive to the skin and irritating to eye.

The potential health hazard of the alkylphenols category members is moderate based on repeated-dose and reproductive toxicity.

No data gaps were identified under the HPV Challenge Program. All HPV Challenge Program endpoints have been adequately addressed by a combination of test data and read across from tested category chemicals to untested category members.

1. Physical-Chemical Properties and Environmental Fate

A summary of physical-chemical properties and environmental fate data submitted is provided in Table 1. For the purpose of the screening-level hazard characterization, the review and summary of these data was limited to the octanol-water partition coefficient and biodegradation endpoints as indictors of bioaccumulation and persistence, respectively.

Octanol-Water Partition Coefficient

o-Substituted Alkylphenols

o-sec-Butylphenol (CAS No. 89-72-5)
Log K_{ow}: 3.46 (estimated)

2-tert-Butylphenol (CAS No. 88-18-6)
Log K_{ow}: 3.31

p-Substituted Alkylphenols

p-tert-Butylphenol (CAS No. 98-54-4)
Log K_{ow}: 3.31 (measured)

p-sec-Butylphenol (CAS No. 99-71-8)
Log K_{ow}: 3.46 (measured)

p-tert-Amylphenol (CAS No. 80-46-6)
Log K_{ow}: 4.03

Heptyl derivatives (p-heptylphenol) (CAS No. 72624-02-3)
Log K_{ow}: 5.01 (estimated)

p-tert-Octylphenol (CAS No. 140-66-9)
Log K_{ow}: 4.12 (measured)

p-Octylphenol (CAS No. 1806-26-4)
Log K_{ow}: 5.50 (estimated)

p-(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 599-64-4)
Log K_{ow}: 4.12 (estimated)

p-Nonylphenol (CAS No. 84852-15-3)
Log K_{ow}: 3.28 (measured)

p-Dodecylphenol (CAS No. 210555-94-5)
Log K_{ow}: 7.17 (estimated)

Di- and Tri-Substituted Mixed Alkylphenols

2,3,6-Trimethylphenol (CAS No. 2416-94-6)
Log K_{ow}: 2.72 (measured)

2,4-Di-tert-butylphenol (CAS No. 96-76-4
Log K_{ow}: 5.33 (estimated)

2,6-Di- tert-butylphenol (CAS No. 128-39-2)
Log K_{ow}: 4.5 (measured)

2,4-Di-tert-pentylphenol (CAS No. 120-95-6)
Log K_{ow}: 6.31 (estimated)

4-sec-Butyl-2,6-tert-butylphenol (CAS No. 17540-75-9)
Log K_{ow}: 6.43 (estimated)

2,4,6-Tri-tert-butylphenol (CAS No. 732-26-3)
Log K_{ow}: 6.06 (measured)

2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 2772-45-4)
Log K_{ow}: 6.73 (estimated)

Biodegradation

o-Substituted Alkylphenols

No measured biodegradation data were provided for these chemicals. Biodegradation estimates, generated by BIOWIN, were provided to support evaluation of biodegradation.
***o*-Substituted alkyphenols are not readily biodegradable.**

p-Substituted Alkylphenols

p-tert-Butylphenol (, CAS No. 98-54-4)
In a DOC Die Away test, the inoculum was non-adapted, domestic, activated sludge. After 28 days, 98% of the test substance had degraded.
***p-tert*-Butylphenol is readily biodegradable.**

p-sec-Butylphenol (CAS No. 99-71-8)
In a CO_2 Evolution test, the inoculum was non-adapted, domestic, activated sludge. After 28 days, 67% of the test substance had degraded.
***p-sec*-Butylphenol is readily biodegradable.**

p-Octylphenol (CAS No. 1806-26-4)
A modified MITI Test (II) for inherent biodegradability of *p*-octylphenol (CAS No. 1806-26-4) was evaluated using non-adapted organisms from activated sludge. After 28 days, 0% of the test substance had degraded.
***p*-Octylphenol is not readily biodegradable.**

p-tert-Amylphenol (CAS No. 80-46-6)
Heptyl derivatives (p-heptylphenol) (CAS No. 72624-02-3)
p-tert-Octylphenol (CAS No. 140-66-9)
p-(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 599-64-4)
p-Nonylphenol (CAS No. 84852-15-3)
p-Dodecylphenol (CAS No. 210555-94-5)
Measured biodegradation data were not provided for the remaining six chemicals in this subcategory. Biodegradation estimates, generated by BIOWIN, were provided to support evaluation of biodegradation for these chemicals.
These *p*-Substituted alkyphenols are not readily biodegradable.

Di- and Tri-Substituted Mixed Alkylphenols

2,3,6-Trimethylphenol (CAS No. 2416-94-6)
A Zahn-Wellens Test for inherent biodegradability was conducted using activated sludge. After 28 days, 98% of the test substance had degraded. 2,3,6-Trimethylphenol is inherently but not readily biodegradable.
***2,3,6*-Trimethylphenol is not readily biodegradable.**

2,6-Di-tert-butylphenol (CAS No. 128-39-2)
A Modified Sturm ready biodegradability test was conducted with bacteria form activated sludge as inoculum. After 28 days, 4% of the test substance had degraded.
2,6-Di-*tert*-butylphenol is not readily biodegradable.

2,4-Di- tert-butylphenol (CAS No. 96-76-4)
2,4-Di-tert-pentylphenol (CAS No. 120-95-6)
4-sec-Butyl-2,6-tert-butylphenol (CAS No. 17540-75-9)
2,4,6-Tri-tert-butylphenol (CAS No. 732-26-3)
2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 2772-45-4)
Measured biodegradation data were not provided for the remaining five chemicals in this subcategory. Biodegradation estimates, generated by BIOWIN, were provided to support evaluation of biodegradation for these chemicals. BIOWIN estimates indicate:
These di- and tri-substituted mixed alkylphenols are not readily biodegradable.

Conclusion: The log K_{ow} of the members of the *o*-substituted alkylphenols subcategory indicates that their potential to bioaccumulate is expected to be low. The log K_{ow} of the members of the *p*-substituted alkylphenols subcategory with the smaller alkyl groups (butyl) indicates that their potential to bioaccumulate is expected to be low; the category members with the larger alkyl substituents have higher log K_{ow} values (mostly above 4) indicating their potential to bioaccumulate is expected to be high. The log K_{ow} of the di- and tri-substituted mixed alkylphenols subcategory members indicates that the potential to bioaccumulate is expected to be high.

o-Substituted alkylphenol subcategory members are not readily biodegradable, indicating that they have the potential to persist in the environment. Of the *p*-substituted alkylphenol subcategory members, *p-tert*-butylphenol and *p-sec*-butylphenol, are readily biodegradable, indicating that they do not have the potential to persist in the environment. All other *p*-substituted alkylphenol subcategory members are not readily biodegradable, indicating that they have the potential to persist in the environment. Di- and tri-substituted mixed alkylphenols subcategory members are not readily biodegradable, indicating that they have the potential to persist in the environment.

Table 1. Summary of Physical-Chemical Properties and Environmental Fate Data

Chemical	Melting point (ºC)	Boiling Point (ºC)	Vapor Pressure (hPa at 25ºC)	Log K_{ow}	Water Solubility (mg/L at 25ºC)
***o*-Substituted Alkylphenols**					
***o*-*sec*-Butylphenol (CAS No. 89-72-5)**	**14 (m)**	**224 (m)**	0.023 (e)	3.46 (e)	319 (e)
2-*tert*-Butylphenol (CAS No. 88-18-6)	**-7 (m)**	**223 (m)**	**0.12 (m)**	3.31	331 (e)
***p*-Substituted Alkylphenols**					
***p*-*tert*-Butylphenol (CAS No. 98-54-4)**	**100 (m)**	**237 (m)**	**0.005 (m)**	**3.31 (m)**	**800 (m) @ 20 ºC**
***p*-*sec*-Butylphenol (CAS No. 99-71-8)**	**56 (m)**	**239 (m)**	4.9×10^{-3}	**3.46 (m)**	**960 (m)**
***p*-*tert*-Amylphenol (CAS No. 80-46-6)**	**95 (m)**	**263 (m)**	0.001 (e)	4.03	168
Heptyl derivatives (*p*-heptylphenol) (CAS No. 72624-02-3)	73 (e)	**256 – 280 (m)**	**0.0113 (m)**	5.01(e)	122
***p*-tert-Octylphenol (CAS No. 140-66-9)**	**81 (m)**	**282 (m)**	**0.0021 (m)**	**4.12 (m)**	18
***p*-octylphenol (CAS No. 1806-26-4)**	83 (e)	**296 (m)**	1.3×10^{-4} (e)	5.50 (e)	3.11 (e)
***p*-(alpha, alpha-Dimethylbenzyl)phenol or *p*-cumylphenol (CAS No. 599-64-4)**	**72 (m)**	**335 (m)**	3.0×10^{-5} (e)	4.12 (e)	43.3 (e)
***p*-Nonylphenol (CAS No. 84852-15-3)**	**25 (m)**	**310 (m)**	**4.6×10^{-5} (m)**	**3.28 (m)**	3.93
***p*-Dodecylphenol (CAS No. 210555-94-5)**	**-9 (m)**	**308 (m)**	**9.19×10^{-5} (m)**	7.17 (e)	2.1
Di- and Tri-Substituted Mixed Alkylphenols					
2,3,6-Trimethylphenol (CAS No. 2416-94-6)	**65 (m)**	**222 (m)**	< 0.110	**2.72 (m)**	1420
2,4-Di-*tert*-butylphenol (CAS No. 96-76-4)	**57 (m)**	**264 (m)**	0.01	5.33 (e)	12
2,6-Di-*tert*-butylphenol (CAS No. 128-39-2)	**37 (m)**	**253 (m)**	0.01	**4.5 (m)**	4.11
2,4-Di-*tert*-pentylphenol (CAS No. 120-95-6)	**26 (m)**	311 (e)	$1x10^{-4}$ (e)	6.31 (e)	0.444 (e)
4-*sec*-Butyl-2,6-tert-butylphenol (CAS No. 17540-75-9)	**47 (m)**	**275 (m)**	2.8×10^{-5}	6.43 (e)	0.248 (e)
2,4,6-Tri-*tert*-butylphenol (CAS No. 732-26-3)	**131 (m)**	**278 (m)**	8.8×10^{-2}	**6.06 (m)**	0.267 (e)
2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 2772-45-4)	**65 (m)**	**> 300 (m)**	7.8×10^{-7} Pa (e)	6.73 (e)	0.055 (e)

Chemical	Stability in Water (Hydrolysis) (year)	Direct Photo-degradation (cm^3/molecule-sec)	Indirect (OH^-) Photo-degradation $t_{1/2}$ (h)	Fugacity (Level III Model)				Biodegradation
				Soil (%)	Water (%)	Sediment (%)	Air (%)	
***o-sec*-Butylphenol (CAS No. 89-72-5)**	Hydrolysis is not expected because lacks hydrolyzable functional groups	Not susceptible to direct photolysis	Indirect photolysis via reaction from hydroxyl radicals is rapid	56.7	34.4	1.26	7.6	Not readily biodegradable (e)
2-*tert*-Butylphenol (CAS No. 88-18-6)				46.3	25.6	1.03	27.0	Not readily biodegradable (e)
***p-tert*-Butylphenol (CAS No. 98-54-4)**	Hydrolysis is not expected because lacks hydrolyzable functional groups	Not susceptible to direct photolysis	Indirect photolysis via reaction from hydroxyl radicals is rapid	80.5	18.4	0.85	0.26	**98 % (m)** Readily biodegradable
***p-sec*-Butylphenol (CAS No. 99-71-8)**				73.8	25.1	0.49	0.6	**67% (m)** Readily biodegradable
***p-tert*-Amylphenol (CAS No. 80-46-6)**				79.4	17.1	3.27	0.25	Not readily biodegradable (e)
Heptyl derivatives (*p*-heptylphenol) (CAS No. 72624-02-3)				96.6	1.07	2.15	0.16	Not readily biodegradable (e)
***p-tert*-Octylphenol (CAS No. 140-66-9)**				53.3	9.07	37.5	0.17	Not readily biodegradable (e)
***p*-Octylphenol (CAS No. 1806-26-4)**				48.0	12.4	39.3	0.32	**0% (m)** Not readily biodegradable
***p*-(alpha, alpha-Dimethyl-benzyl)phenol or *p*-cumylphenol (CAS No. 599-64-4)**				80.0	15.1	4.72	0.17	Not readily biodegradable (e)
***p*-Nonylphenol (CAS No. 84852-15-3)**				36.9	4.47	58.5	0.10	Not readily biodegradable (e)
***p*-Dodecylphenol (CAS No. 210555-94-5)**				28.7	2.07	69.2	0.07	Not readily biodegradable (e)
2,3,6-Trimethylphenol (CAS No. 2416-94-6)	Hydrolysis is not expected because lacks hydrolyzable functional groups	Not susceptible to direct photolysis	Indirect photolysis via reaction from hydroxyl radicals is rapid	27.9	59.9	0.62	11.6	**98% (m)** Not readily biodegradable
2,4-Di-*tert*-butylphenol (CAS No. 96-76-4)				95.6	0.50	2.12	1.75	Not readily biodegradable (e)
2,6-Di-*tert*-butylphenol (CAS No. 128-39-2)				70.3	2.51	1.56	25.6	**4% (m)** Not readily biodegradable
2,4-Di-*tert*-pentylphenol (CAS No. 120-95-6)				97.6	0.06	2.17	0.06	Not readily biodegradable (e)
4-*sec*-Butyl-2,6-tert-butylphenol (CAS No. 17540-75-9)				97.6	0.06	2.17	0.06	Not readily biodegradable (e)
2,4,6-Tri-*tert*-butylphenol (CAS No. 732-26-3)				96.1	0.1	2.13	1.65	Not readily biodegradable (e)
2,4-bis(alpha, alpha-Dimethyl-benzyl) phenol (CAS No. 2772-45-4)				97.7	0.02	2.17	0.0	Not readily biodegradable (e)

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

2. Environmental Effects – Aquatic Toxicity

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 2. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Toxicity to Fish

o-Substituted Alkylphenols

o-sec-Butylphenol (CAS No. 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, was provided to support evaluation of the acute toxicity.
96-h LC_{50} = 2.78 mg/L

2-tert-Butylphenol (CAS No. 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, was provided to support evaluation of the acute toxicity.
96-h LC_{50} = 2.9 mg/L

p-Substituted Alkylphenols

p-tert-Butylphenol (CAS No. 98-54-4)
(1) 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.
96-h LC_{50} = 5.1 mg/L

(2) Fathead minnows (*P. promelas*) were exposed to *p-tert*-butylphenol (concentrations not provided) under flow-through conditions for 96 hours.
96-h LC_{50} = 5.14 mg/L

p-sec-Butylphenol (CAS No. 99-71-8)
Juvenile Atlantic salmon (*Salmo salar*) 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 (CAS No. 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, was provided to evaluate the acute toxicity of *p-tert*-amylphenol.
96-h EC_{50} = 1.6 mg/L

p-Heptylphenol (CAS No. 72624-02-3)
Groups of rainbow trout (*Oncorhynchus mykiss*) 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 (CAS No. 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, 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 early life-stage test, rainbow trout (*Salmo gairdneri*) eggs were exposed to *p-tert*-octylphenol at nominal concentrations of 0.0062, 0.012, 0.025, 0.050 and 0.10 mg/L (0.011, 0.022, 0.051 and 0.091 mg/L, measured) under flow-through conditions.
60-d NOEC = 0.0061 mg/L

p-Octylphenol (CAS No. 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, was provided to evaluate the acute toxicity of *p*-octylphenol.
96-h EC_{50} = 0.21 mg/L

p-(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 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, was provided to evaluate the acute toxicity of *p*-(alpha, alpha-dimethylbenzyl)phenol.
96-h EC_{50} = 1.5 mg/L

p-Nonylphenol (CAS No. 84852-15-3)
(1) Sheepshead minnows (*Cyprinodon variegates*) were exposed to *p*-nonylphenol at nominal concentrations of 0.075, 0.125, 0.19, 0.31 and 0.5 mg/L for 96 hours.
96-h LC_{50} = 0.31 mg/L

(2) Fathead minnows (*P. promelas*) were exposed to *p*-nonylphenol for 96 hours (test concentrations not provided in robust summary)
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 3.0, 6.0, 9.0, 15 and 25 µg/L.
33-d NOEC = 0.0074 mg/L

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

p-Dodecylphenol (CAS No. 210555-94-5)
(1) 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

(2) 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

(3) A 96-hour EC_{50} for fish, estimated by ECOSAR, was provided to evaluate the acute toxicity of *p*-dodecylphenol.
96-h EC_{50} = 0.025 mg/L

Di- and Tri-Substituted Mixed Alkylphenols

2,3,6-Trimethylphenol (CAS No. 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 (mean = 16 mg/L)

(2) In another study, fathead minnows were exposed to 2,3,6-trimethylphenol under flow-through conditions. No details regarding the study were provided.
96-h LC_{50} = 8.2 mg/L

2,4-Di-tert-butylphenol (CAS No. 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, was provided to evaluate the acute toxicity of 2,4-di-*tert*-butylphenol.
96-h EC_{50} = 0.27 mg/L

2,6-Di-tert-butylphenol (CAS No. 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.
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.
96-h LC_{50} = 10 mg/L

(4) Rainbow trout (*O. mykiss*) were exposed to 2,6-di-*tert*-butylphenol at 0, 0.21., 0.28, 0.43, 0.66 and 1.0 mg/L under flow-through conditions for 14 days.
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 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 (CAS No. 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, was provided to evaluate the acute toxicity of 2,4-di-*tert*-pentylphenol.
96-h EC_{50} = 0.076 mg/L

4-sec-Butyl-2,6-tert-butylphenol (CAS No. 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, was provided to evaluate the acute toxicity of 4-*sec*-butyl-2,6-*tert*-butylphenol.
96-h EC_{50} = 0.072 mg/L

2,4,6-Tri-tert-butylphenol (CAS No. 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, was provided to evaluate the acute toxicity of 2,4,6-tri-*tert*-butylphenol.
96-h EC_{50} = 0.076 mg/L

2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 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, was provided to evaluate the acute toxicity of 2,4-bis(alpha, alpha-dimethylbenzyl)phenol.
96-h EC_{50} = 0.059 mg/L

Acute Toxicity to Aquatic Invertebrates

o-Substituted Alkylphenols

o-sec-Butylphenol (CAS No. 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, was provided to evaluate the acute toxicity of *o-sec*-butylphenol.
48-h EC_{50} = 2.0 mg/L

2-tert-Butylphenol (CAS No. 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, was provided to evaluate the acute toxicity of 2-*tert*-butylphenol.
48-h EC_{50} = 2.1 mg/L

p-Substituted Alkylphenols

p-tert-Butylphenol (CAS No. 98-54-4)
(1) *Daphnia magna* (20 per concentration) 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.
24-h EC_{50} = 7.3 mg/L
48-h EC_{50} = 6.7 mg/L
NOEC < 1.0 mg/L

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

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

(4) *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 (CAS No. 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, was provided to evaluate the acute toxicity of *p-sec*-butylphenol.
48-h EC_{50} = 2.05 mg/L

p-tert-Amylphenol (CAS No. 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) *C. septemspinosa* (shrimp) were exposed to *p-tert*-amylphenol for 96 hours; test conditions were not provided.
96-h LC_{50} = 0.3 mg/L

(3) 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, was provided to evaluate the acute toxicity of *p-tert*-amylphenol.
48-h EC_{50} = 1.5 mg/L

Heptyl derivatives (p-heptylphenol) (CAS No. 72624-02-3)
(1) 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, was provided to evaluate the acute toxicity of *p-tert*-amylphenol.
48-h EC_{50} = 0.61 mg/L

p-tert-Octylphenol (CAS No. 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.
24-h LC_{50} = 0.26 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, 0.26 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 (CAS No. 1806-26-4)
A standard acute toxicity test for aquatic invertebrates was not provided for *p*-octylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR, was provided to evaluate the acute toxicity of *p*-octylphenol.
48-h EC_{50} = 0.41 mg/L

p-(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 599-64-4)
A standard acute toxicity test for aquatic invertebrates was not provided for *p*-cumylphenol. A 48-hour EC_{50} for *Daphnia*, estimated by ECOSAR, was provided to evaluate the acute toxicity of *p*-cumylphenol.
48-h EC_{50} = 1.6 mg/L

p-Nonylphenol (CAS No. 84852-15-3)
(1) *D. magna* were exposed to *p*-nonylphenol for 48-hours; test conditions were not provided. Solvent (acetone) used in the test, but no solvent control 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) *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 = 0.015 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) *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 (CAS No. 210555-94-5)
(1) *Daphnia magna* were exposed to *p*-dodecylphenol under static conditions for 48 hours.
24-h EC_{50} = 0.11 mg/L
48-h EC_{50} = 0.093 mg/L

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

Di- and Tri-Substituted Mixed Alkylphenols

2,3,6-Trimethylphenol(CAS No. 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} = 0.143 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, was provided to evaluate the acute toxicity of 2,3,6-trimethylphenol.
48-h EC_{50} = 2.5 mg/L

2,4-Di-tert-butylphenol (CAS No. 96-76-4)
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, was provided to evaluate the acute toxicity of 2,4-di-tert-butylphenol.
48-h EC_{50} = 0.48 mg/L

2,6-Di-tert-butylphenol (CAS No. 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.
24-h EC_{50} > 0.59 mg/L
48-h EC_{50} > 0.45 mg/L
48-h NOEC = 0.076 mg/L

(4) *Gammarus fasciatus* were exposed to 2,6-di-*tert*-butylphenol under flow-through conditions for 96 hours.
24-h LC_{50} = 1.0 mg/L
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

2,4-Di-tert-pentylphenol (CAS No. 120-95-6)
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, was provided to evaluate the acute toxicity of 2,4-di-*tert*-pentylphenol.
48-h EC_{50} = 0.22 mg/L

4-sec-Butyl-2,6-tert-butylphenol (CAS No. 17540-75-9)
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, was provided to evaluate the acute toxicity.
48-h EC_{50} = 0.22 mg/L

2,4,6-Tri-tert-butylphenol (CAS No. 732-26-3)
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, was provided to evaluate the acute toxicity of 2,4,6-tri-*tert*-butylphenol.
48-h EC_{50} = 0.226 mg/L

2,4-bis(alpha, alpha-Dimethylbenzyl)phenol CAS No. 2772-45-4)
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, was provided to evaluate the acute toxicity of 2,4-bis(alpha, alpha-dimethylbenzyl)phenol.
48-h EC_{50} = 0.21 mg/L

Toxicity to Aquatic Plants

o-Substituted Alkylphenols

o-sec-Butylphenol (CAS No. 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, was provided to evaluate the plant toxicity of *o-sec*-butylphenol.
96-h EC_{50} = 3.8

2-tert-Butylphenol (CAS No. 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, was provided to evaluate the plant toxicity of 2-*tert*-butylphenol.
96-h EC_{50} = 4.1

p-Substituted Alkylphenols

p-tert-Butylphenol (CAS No. 98-54-4)
(1) Green algae (*Scenedesmus subspicatus*) were exposed to *p-tert*-butylphenol under static (open-system) conditions for 72 hours.
72-h EC_{50} (biomass) = 22.7 mg/L
72-h NOEC (biomass) = 9.53 mg/L

(2) *Chlorella vulgaris* were exposed to *p-tert*-butylphenol for 6 hours; test conditions were not provided.
6-h EC_{50} (growth inhibition) = 22.2 - 34.4 mg/L

p-sec-Butylphenol (CAS No. 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, was provided to evaluate the plant toxicity of *p-sec*-butylphenol.
96-h EC_{50} = 3.81

p-tert-Amylphenol (CAS No. 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, was provided to evaluate the plant toxicity of *p-tert*-amylphenol.
96-h EC_{50} = 1.7

Heptyl derives (p-heptylphenol) (CAS No. 72624-02-3)
(1) Green algae (*S. subspicatus*) were exposed to *p*-heptylphenol under static conditions for 96 hours.
96-h EC_{50} (biomass) = 0.83 mg/L
96-h EC_{50} (growth) = 2.5 mg/L

p-tert-Octylphenol (CAS No. 140-66-9)
(1) Green algae (*S. subspicatus*) 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} = 1.9 mg/L
96-h NOEC < 1.0 mg/L

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

p-Octylphenol (CAS No. 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 plant toxicity of *p*-octylphenol.
96-h EC_{50} = 0.082 mg/L

p-(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 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, was provided to evaluate the plant toxicity of *p*-cumylphenol.
96-h EC_{50} = 14 mg/L

p-Nonylphenol (CAS No. 84852-15-3)
(1) Green algae (*S. subspicatus*) were exposed to *p*-nonylphenol under static conditions for 96 hours. Robust summary reports analytical monitoring was conducted; however, reports nominal concentrations as 0, 0.0, 6, 0.12, 0.25 and 0.5 mg/L.
96-h EC_{50} = 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) *Skeletonema costatum* (saltwater) was exposed to *p*-nonylphenol under static conditions for 96 hours.
96-h EC_{50} (growth) = 0.027 mg/L

p-Dodecylphenol (CAS No. 210555-94-5)
(1) Green algae (*S. subspicatus)* were exposed to *p*-dodecylphenol under static conditions for 72 hours.
72-h EC_{50}= 0.77 mg/L
72-h NOEC= 0.44 mg/L

(2) A standard toxicity test for aquatic plants was not provided for *p*-dodecylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR, was provided to evaluate the plant toxicity of *p*-dodecylphenol.
96-h EC_{50} = 0.003 mg/L

Di- and Tri-Substituted Mixed Alkylphenols

2,3,6-Trimethylphenol (CAS No. 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 standard toxicity test for aquatic plants was not provided for 2,3,6-trimethylphenol. A 96-hour EC_{50} for green algae, estimated by ECOSAR, was provided to evaluate the plant toxicity of 2,3,6-trimethylphenol.
96-h EC_{50} = 6.4 mg/L

2,4-Di-tert-butylphenol (CAS No. 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, was provided to evaluate the plant toxicity of 2,4-di-*tert*-butylphenol.
96-h EC_{50} = 0.12 mg/L

2,6-Di- tert-butylphenol (CAS No. 128-39-2)
(1) Green algae (*S. subspicatus*) 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.
24-h EC_{50} = .086 mg/L
48-h EC_{50} = 0.50 mg/L
72-h EC_{50} = 0.51 mg/L
96-h EC_{50} (growth) = 0.56 mg/L

(2) Green algae (*Scenedesmus subspicatus*) 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.
24-h EC_{50} = 1.7 mg A.I./L
48-h EC_{50} = 1.7 mg A.I./L
72-h EC_{50} = 1.4 mg A.I./L
96-h EC_{50} = 1.2 mg A.I./L
96-h NOEC (growth) = 0.64 mg A.I./L

2,4-Di-tert-pentylphenol (CAS No. 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, was provided to evaluate the plant toxicity of 2,4-di-*tert*-pentylphenol.
96-h EC_{50} = 0.018 mg/L

4-sec-Butyl-2,6-tert-butylphenol (CAS No. 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, was provided to evaluate the plant toxicity of 4-*sec*-butyl-2,6-*tert*-butylphenol.
96-h EC_{50} = 0.016 mg/L

2,4,6-Tri-tert-butylphenol (CAS No. 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, was provided to evaluate the plant toxicity of 2,4,6-tri-*tert*-butylphenol.
96-h EC_{50} = 0.017 mg/L

2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 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, was provided to evaluate the plant toxicity of 2,4-bis(alpha, alpha-dimethylbenzyl)phenol.
96-h EC_{50} = 0.011 mg/L

Conclusion: The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of *o*-substituted alkylphenols subcategory to aquatic organisms is moderate.

The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of the majority of *p*-substituted alkylphenols subcategory to aquatic organisms is moderate. A few of the category members have high aquatic plant toxicity values, indicating that they pose a high hazard to aquatic plants. The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of di- and tri-substituted mixed alkylphenols subcategory to aquatic organisms is moderate to high. Generally, the hazard potential for the category members with smaller substituents is moderate. Estimated toxicity values for category members with larger substituents indicate high potential hazard for fish and aquatic plants.

Table 2. 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*-*sec*-Butylphenol (CAS No. 89-72-5)**	2.8 (e)	**1.3(m)** 2.0 (e)	3.8(e)	—
2-*tert*-Butylphenol (CAS No. 88-18-6)	**15.5 (m)**[1] 2.9 (e)	**2.4 (m)** 2.1 (e)	4.1(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)**	—
***p*-*sec*-Butylphenol (CAS No. 99-71-8)**	**0.74 (m)**	**1.8 (m)** (96-h) 2.05 (e)	3.81(e)	—
***p*-*tert*-Amylphenol (CAS No. 80-46-6)**	1.6 (e)	**0.3–1.7 (m)** (96-h) 1.5 (e) (48-h)	1.7 (e)	—
Heptyl derivatives (*p*-heptylphenol) (CAS No. 72624-02-3)	**0.85 (m)**	0.6 (e) (48-h)	**0.83 (m)** (biomass) **2.5 (m)** (growth)	—
***p*-*tert*-Octylphenol (CAS No. 140-66-9)**	**0.25 (m)**	**0.27 (m)**	**1.9 (m)** **1.1 (m)** (72-h)	**60-d fish = 0.0061 (m)** **21-d daphnid = 0.037(m)**
***p*-Octylphenol (CAS No. 1806-26-4)**	0.21 (e)	0.41 (e)	0.082 (e)	—
***p*-(alpha, alpha-Dimethylbenzyl)phenol or *p*-cumylphenol (CAS No. 599-64-4)**	1.5 (e)	1.6 (e)	14 (e)	—
***p*-Nonylphenol (CAS No. 84852-15-3)**	**0.128 – 0.31 (m)**	**0.085 – 0.19 (m)**	**0.027 – 0.41 (m)** **0.0563 (m) (72-h)**	**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)**	**0.093 (m)** **0.15 (m) (96-h)**	**0.77 (m) (72-h)** 0.003 (e)	—
Di- and Tri--Substituted Mixed Alkylphenols				
2,3,6-Trimethylphenol (CAS No. 2416-94-6)	**8.2 – 16 (m)**	**12.6 (m) (24-h)** 2.5 (e)	**19 (m) (72-h)** 6.4 (e)	—
2,4-Di-*tert*-butylphenol (CAS No. 96-76-4)	**1.8 (m) (48-h)** 0.27 (e)	0.48 (e)	0.12 (e)	—
2,6-Di-*tert*-butylphenol (CAS No. 128-39-2)	**1.4 – 10 (m)**	**> 0.45–0.80 (m)** **1.7–5.5 (m;24-h)**	**0.5 – 1.2 (m)**	—
2,4-Di-*tert*-pentylphenol (CAS No. 120-95-6)	0.076 (e)	0.22 (e)	0.018 (e)	—
4-*sec*-Butyl-2,6-*tert*-butylphenol (CAS No. 17540-75-9)	0.072 (e)	0.22 (e)	0.016 (e)	—
2,4,6-Tri-*tert*-butylphenol (CAS No. 732-26-3)	0.076 (e)	0.23 (e)	0.017 (e)	—
2,4-bis(alpha, alpha)Dimethylbenzyl)-phenol (CAS No. 2772-45-4)	0.059 (e)	0.21 (e)	0.011 (e)	—

(m) = measured data (i.e. derived from testing); (e) = estimated data (i.e., derived from modeling);
[1]compound tested was an unspecified mixture containin 2.27% 2-*tert*-butylphenol

3. Human Health Effects

A summary of health effects data submitted for SIDS endpoints is provided in Table 3. 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

The members of the *o*-substituted alkylphenols subcategory have low acute oral toxicity and moderate acute dermal toxicity. The oral LD_{50} values range from > 200 to 2700 mg/kg-bw, collectively indicating low hazard via oral exposure. The dermal LD_{50} value available for 2-*tert*-butylphenol indicates moderate hazard via dermal exposure. Available LD_{50} values for individual subcategory members are provided in Table 3.

p-Substituted Alkylphenols

The members of the *p*-substituted alkylphenols subcategory have low acute oral toxicity and low acute dermal toxicity. 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, collectively indicating low hazard via oral exposure. The dermal LD_{50} value is > 2000 mg/kg-bw, indicating low hazard via dermal exposure. Available LD_{50} values for individual subcategory members are provided in Table 3.

Di- and Tri-Substituted Mixed Alkylphenols

The members of the di- and tri-substituted mixed alkylphenols subcategory have low acute oral toxicity and moderate acute dermal toxicity. Acute oral toxicity data are available for all but one member of 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, indicating low hazard via oral exposure. The dermal LD_{50} value is > 1000 mg/kg-bw, indicating moderate hazard via dermal exposure. 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 (CAS No. 89-72-5) and 2-*tert*-butylphenol (CAS NO. 88-18-6).

p-Substituted Alkylphenols

p-tert-Butylphenol (CAS No. 98-54-4)

(1) In a 14-day range-finding study (for the definitive study below), male and female rats were administered *p-tert*-butylphenol daily via gavage in 0.5% aqueous methyl cellulose at 0, 250, 500 and 1000 mg/kg-bw/day. 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 rats were administered *p-tert*-butylphenol via gavage in 0.5% aqueous methyl cellulose at 0, 20, 60 and 200 mg/kg-bw/day. No treatment-related changes were observed except noisy respiratory sounds in females of the high-dose group. In males of the high-dose group, only plasma albumin level was decreased.

LOAEL = Not established

NOAEL = 200 mg/kg-bw/day (highest dose tested)

(3) Male Syrian Hamsters were administered *p-tert*-butylphenol in the diet at 15,000 ppm (approximately 600 mg/kg-bw/day) for 20 weeks. At the end of the study, there was a decrease in average body weight (by 5%) and absolute 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 hyperplasia was statistically significant ($p < 0.01$ to $p < 0.001$). No abnormal findings were seen in liver, kidney, cheek pouch, lungs, pancreas and urinary bladder.
LOAEL = 15,000 ppm (approximately 600 mg/kg-bw/day; based on liver weight change**)**
NOAEL = Not established

p-tert-Octylphenol (CAS No. 140-66-9)
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. No effects were seen on survival, growth, food consumption, urinary excretion of glucose and protein, hematological parameters, or organ weights or histopathology.
LOAEL = Not established
NOAEL = 5% (approximately 2500 mg/kg-bw/day; highest dose tested**)**

p-Nonylphenol (CAS No. 54852-15-3)
(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 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, and minor vacuolation in the periportal hepatocytes in the liver. No such effects were seen in females.
LOAEL = 400 mg/kg-bw/day (based on effects on kidney, liver and testes and changes in clinical chemistry parameters)
NOAEL = 100 mg/kg-bw/day

(2) Groups of Crl:CD BR 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. 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 weights and food consumption was noted in the 150 mg/kg-bw/day. At week 14, a dose-related increase in kidney weights 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. Since these changes were of small magnitude and there were no corresponding clinical or histopathological changes, the findings were not considered toxicologically significant. 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 dose-related effects on kidney**)**
NOAEL = Not established

Di- and Tri-Substituted Mixed Alkylphenols

***2,6-Di-tert-butylphenol* (CAS No. 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 total protein males and females and increased albumin level in males were also seen. Enlarged cecum 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. A slight increase in the incidence of hepatocellular hypertrophy in the centrilobular area in males and female 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.
LOAEL = 100 mg/kg-bw/day (based on increased relative liver weights and enlarged cecum in males)
NOAEL = 15 mg/kg-bw/day

***2,4,6-Tri-tert-butylphenol* (CAS No. 732-26-3)**
Male and female Wistar rats 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. Increase in relative liver (male and female at 300 and 1000 ppm) and absolute kidney weights (male and female at 100, 300, and 1000 ppm) and increase in adrenal weights (male and female: swelling, focal necrosis and vacuolization of liver cells were seen in the 300 and 1000 groups).
LOAEL = 100 ppm (approximately 5 mg/kg-bw/day; based on liver effects, kidney weights and increases in cholesterol and platelets)
NOAEL = 30 ppm (approximately 1.5 mg/kg-bw/day)

Reproductive Toxicity

<u>p-Substituted Alkylphenols</u>

p-tert-Butylphenol (CAS No. 98-54-4)
In a combined repeated-dose/reproductive/developmental toxicity screening test, male and female rats were administered the test substance 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. No effects on reproduction or developmental parameters were seen.
LOAEL = Not established
NOAEL = 200 mg/kg-bw/day (highest dose tested)

p-tert-Octylphenol (CAS No. 140-66-9)
In a two generation reproduction study, Sprague-Dawley rats (30/sex/group) were administered the test substance 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 and 0.08, 8, 80 and 800 mg/kg-bw/day for weanlings). Dietary administration of *p-tert*-octylphenol for two generations resulted in decreased body weights and weight gains at 2000 ppm. Offspring toxicity was evident at 2000 ppm from decreased body weight during lactation. Delayed vaginal opening and preputial separation at 2000 ppm was seen. The study author related this finding to the reduced body weights. There were no effects o reproductive parameters, testes weights or morphology, epididymal sperm counts, motility or morphology, sperm production, estrogen-like effects on males or females, or effects on prostate weights or histopathology.
LOAEL (parental/offspring toxicity) = 2000 ppm (approximately 100mg/kg-bw/day for males and 150 for females mg/kg-bw/day; based on effects on body weights in parents and offspring and delayed vaginal opening and preputial separation in offspring**)**
NOAEL (parental/offspring toxicity = 200 ppm (approximately 10mg/kg-bw/day for males and 15 for females mg/kg-bw/day)

p-Nonylphenol (CAS No. 54852-15-3)
In a three generation reproduction study, Sprague-Dawley rats were administered diet containing 0, 200, 650 and 2000 ppm (approximately 0, 10, 32.5 and 100 mg/kg/day) from study day 1 until necropsy. Premating exposure for F_0 generation was 6 weeks. F_1 and F_2 generation animals received diet containing the same dose as their parents after weaning. Generations were raised until mating at sexual maturity. Reproductive changes were seen in both male and females at or above 650 ppm. Estrous cycle was lengthened at 2000 ppm and a clear treatment-related change in the day of vaginal opening was seen in all three generations. The acceleration in vaginal opening was taken as indication of the estrogenicity of the test substance. No changes were noted in the remaining reproductive/developmental parameters. There were no clear treatment-related changes in testicular descent, preputial separation or sex ratio. Decreased epididymal sperm density and testicular spermatid head counts were seen in the F_2 generation.
LOAEL (parental/offspring toxicity) = 650 ppm (approximately 32.5 mg/kg-bw/day; based on decreased body weights, accelerated vaginal opening**)**
NOAEL (parental/offspring toxicity) = 200 ppm (approximately 10 mg/kg-bw/day)

Di- and Tri-Substituted Mixed Alkylphenols

2,6-Di-tert-butylphenol (CAS No. 128-39-2)
In a combined reproductive and developmental toxicity screening test in Wistar rats, the dose levels were 0, 30, 150 and 750 mg/kg-bw/day. Animals were dosed throughout the pre-mating and mating period—males received the test substance for further 43 days and females up to day 3 post-partum. A slight body weight reduction was seen in male and female rats at 750 mg/kg-bw/day rats. An increased breeding loss/reduced viability index was seen for females at 750 mg/kg-bw/day. There were no effects noted on macroscopic or microscopic examination.
LOAEL (parental and offspring toxicity) = 750 mg/kg-bw/day (based on effects on body weight and increased breeding loss and reduced viability index)
NOAEL (parental and offspring toxicity) = 150 mg/kg-bw/day

Developmental Toxicity

p-Substituted Alkylphenols

p-tert-Butylphenol (CAS No. 98-54-4)
In a combined repeated-dose/reproductive/developmental toxicity screening test, male and female rats were administered the test substance 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. No effects on reproduction or developmental parameters were seen.
LOAEL = Not established
NOAEL = 200 mg/kg-bw/day (highest dose tested)

p-Nonylphenol (CAS No. 54852-15-3)
Pregnant female Wistar rats were administered the test substance 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
LOAEL (developmental toxicity) = Not established
NOAEL (developmental toxicity) = 300 mg/kg-bw/day (highest dose tested)

Di- and Tri-Substituted Mixed Alkylphenols

2,6-Di-tert-butylphenol (CAS No. 128-39-2)
In a combined reproductive and developmental toxicity screening test, Wistar rats were administered the test substance at 0, 30, 150 and 750 mg/kg-bw/day. Animals were dosed throughout the pre-mating and mating period; males received the test substance for further 43 days and females up to day 3 post-partum. A slight body weight reduction was seen in male and female rats at 750 mg/kg-bw/day. An increased breeding loss/reduced viability index was seen for females at 750 mg/kg-bw/day. There were no effects on macroscopic or microscopic examination. At 750 mg/kg-bw/day, body weight gain of pups was reduced.
LOAEL (maternal/developmental toxicity) = 750 mg/kg-bw/day (based on effects on maternal body weight and increased breeding loss and reduced body weight gain in pups)
NOAEL (maternal/developmental toxicity) = 150 mg/kg-bw/day

Genetic Toxicity – Gene Mutation

o-Substituted Alkylphenols

In vitro

o-sec-Butylphenol (CAS No. 89-72-5)

The mutagenicity potential of *o-sec*-butylphenol was evaluated *in vitro* in *Salmonella typhimurium* (TA100, TA1535, TA98, TA 1538 and TA1537) and *Escherichia 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.

***o-sec*-Butylphenol was not mutagenic in this assay.**

2-tert-Butylphenol (CAS No. 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

In vitro

p-tert-Butylphenol (CAS No. 98-54-4)

The mutagenicity potential of members of *p-tert*-butylphenol was evaluated *in vitro* in *S. typhimurium* (TA100, TA1535, TA98, TA 1538 and TA1537) and/or *E. coli* and mammalian cell lines 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.

***p-tert*-Butylphenol was not mutagenic in this assay.**

p-sec-Butylphenol (CAS No. 99-71-8)

The mutagenicity potential of members of *p-sec*-butylphenol was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and/or *E. coli* and mammalian cell lines 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.

***p-sec*-Butylphenol was not mutagenic in this assay.**

p-tert-Amylphenol (CAS No. 80-46-6)

The mutagenicity potential of members of *p-tert*-amylphenol was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and/or *E. coli* and mammalian cell lines 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.

***p-tert*-Amylphenol was not mutagenic in this assay.**

Heptyl derivatives (p-heptylphenol) (CAS No. 72624-02-3)

The mutagenicity potential of members of heptyl derivatives (*p*-heptylphenol) was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and/or *E. coli* and mammalian cell lines 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.

***p*-Heptylphenol was not mutagenic in this assay.**

p-tert-Octylphenol (CAS No. 140-66-9)
The mutagenicity potential of members of *p-tert*-octylphenol was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and/or *E. coli* and mammalian cell lines 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.
***p-tert*-Octylphenol was not mutagenic in this assay.**

p-(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 599-64-4)
The mutagenicity potential of members of *p*-(alpha, alpha-dimethylbenzyl)phenol was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and/or *E. coli* and mammalian cell lines 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.
***p*-(alpha, alpha-Dimethylbenzyl)phenol was not mutagenic in this assay.**

p-Nonylphenol (CAS No. 84852-15-3)
The mutagenicity potential of members of *p*-nonylphenol was evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and/or *E. coli* and mammalian cell lines 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.
***p*-Nonylphenol was not mutagenic in this assay.**

Di- and Tri-Substituted Mixed Alkylphenols

Data are not available for two, 4-di-*tert*-butylphenol (CAS No. 96-76-4), 2,4-di-*tert*-pentylphenol (CAS No. 120-95-6), 2,4,6-tri-*tert*-butylphenol (CAS No. 732-26-3) and 2,4-di-cumylphenol (CAS No. 2772-45-4). The data for the tested members of the sub category are extrapolated/interpolated to the untested members of this category.

In vitro
2,3,6-Trimethylphenol (CAS No. 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) and/or *E. coli* and mammalian cell lines 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.
2,3,6-Trimethylphenol was not mutagenic in these assays.

2,6-Di- tert-butylphenol (CAS No. 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/or *E. coli* and mammalian cell lines 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.
2,6-Di-*tert*-butylphenol was not mutagenic in these assays.

4-sec-Butyl-2,6-tert-butylphenol (CAS No. 17540-75-9)
The mutagenicity potential of 4-*sec*-butyl-2,6-tert-butylphenol was also evaluated *in vitro* in *S. typhimurium* (TA 100, TA1535, TA98, TA 1538 and TA1537) and/or *E. coli* and mammalian cell lines 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 (CAS No. 89-72-5) and 2-*tert*-butylphenol (CAS NO. 88-18-6).

p-Substituted Alkylphenols

Data are not available for *p-tert*-amylphenol (CAS No. 80-46-6), *p*-heptylphenol (CAS No. 72624-02-3), *p-tert*-octylphenol (CAS No. 140-66-9), *p*-octylphenol (CAS No. 1806-26-4), *p*-cumylphenol (CAS No. 599-64-4), and *p*-dodecylphenol (CAS No. 210555-94-5). The data for the tested members of the sub category are extrapolated/interpolated to the untested members.

In vitro
p-tert-Butylphenol (CAS No. 98-54-4)
In vitro chromosomal aberration testing was conducted in cultured rat liver cells with *p-tert*-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-tert*-Butylphenol did not induce chromosomal aberrations in this assay.**

p-sec-Butylphenol (CAS No. 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 (CAS No. 96-76-4); 2,4-di-*tert*-pentylphenol (CAS No. 120-95-6); 2,4,6-tri-*tert*-butylphenol (CAS No. 732-26-3); 2,3,6-Trimethylphenol (CAS No. 2416-94-6); and 2,4-di-cumylphenol (CAS No. 2772-45-4). The data for the tested members of the sub category are extrapolated/interpolated to the untested members.

In vitro
2,6-Di- tert-butylphenol (CAS No. 128-39-2)
In vitro chromosomal aberration testing was conducted in Chinese Hamster V79 cells with 2,6-di- *tert*-butylphenol (CAS No. 128-39-2) 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.
***2,6-Di- tert*-butylphenol did not induce chromosomal aberrations in this assay.**

4-sec-Butyl-2,6-tert-butylphenol (CAS No. 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

<u>p-Substituted Alkylphenols</u>

In vivo
p-Nonylphenol (CAS No. 84852-15-3)
p-Nonylphenol was evaluated in *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

All members of the alkylphenol category are highly irritating or corrosive to skin and irritating to eyes.

Conclusion: The acute oral toxicity for the members of this category is low to moderate. Repeated exposures via the oral route of exposure resulted in effects on liver, kidney, testes and forestomach. Two- and three-generation reproduction toxicity studies indicated no treatment-related effects on reproductive or developmental endpoints, except body weight effects, in parents or offspring. No abnormalities in fetuses were reported for any alkylphenol category member. None of the category members showed mutagenic potential when tested in *Salmonella typhimurium*. No chromosomal aberrations were observed in cells tested with or without metabolic activation for any of the category members. When tested in vivo in a mouse micronucleus assay, *p*-nonylphenol did not induce cytogenetic damage. The category members are considered irritating to corrosive to the skin and irritating to eyes.

The potential health hazard of the alkylphenols category is moderate based on the limited data available for repeated-dose and reproductive toxicity.

Table 3. Summary of Human Health Data

Chemical	Acute Oral Toxicity LD_{50} (mg/kg-bw)	Acute Dermal Toxicity LD_{50} (mg/kg-bw)	Acute Inhalation Toxicity LC_{50} (mg/L/6h/day)	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*-Substituted Alkylphenols**							
***o*-*sec*-Butylphenol (CAS No. 89-72-5)**	**> 200 & < 2000 2700**	No Data 1373 705 (RA)	—	No Data	No Data	No Data	No Data
2-*tert*-Butylphenol (CAS No. 88-18-6)	**789**	**1373 705**	—	No Data	No Data	No Data	No Data
***p*-Substituted Alkylphenols**							
***p*-*tert*-Butylphenol (CAS No. 98-54-4)**	**> 2000 4000 3620 5360**	No Data > 2000 (RA)	No Data	**NOAEL = 200 LOAEL ~ 600**	**NOAEL = 200**	**NOAEL = 200**	No Data LOAEL = 300 (RA)
***p*-*sec*-Butylphenol (CAS No. 99-71-8)**	**1650**	No Data > 2000 (RA)	No Data	No Data NOAEL = 200 LOAEL ~ 600 (RA)	No Data NOAEL = 200 (RA)	No Data NOAEL = 200 (RA)	No Data LOAEL = 300 (RA)
***p*-*tert*-Amylphenol (CAS No. 80-46-6)**	**1830**	No Data > 2000 (RA)	No Data	No Data NOAEL = 200 LOAEL ~ 600 (RA)	No Data NOAEL = 200 (RA)	No Data NOAEL = 200 (RA)	No Data LOAEL = 300 (RA)
Heptyl derivatives (*p*-heptylphenol) (CAS No. 72624-02-3)	**> 200 & < 2000**	**> 2000**	No Data	No Data NOAEL ~ 2500 LOAEL = Not established (RA)	No Data NOAEL ~ 10 LOAEL = 100 (RA)	No Data NOAEL = 75 LOAEL > 300 (RA)	No Data LOAEL = 300 (RA)
***p*-*tert*-Octylphenol (CAS No. 140-66-9)**	**2200**	No Data > 2000 (RA)	No Data	**NOAEL ~ 2500 LOAEL = Not established**	**NOAEL ~ 10 LOAEL = 100**	No Data NOAEL = 75 LOAEL > 300 (RA)	No Data LOAEL = 300 (RA)
***p*-Octylphenol (CAS No. 1806-26-4)**	**1200**	No Data > 2000 (RA)	No Data	No Data NOAEL ~ 2500 LOAEL = Not established (RA)	No Data NOAEL ~ 10 LOAEL = 100 (RA)	No Data NOAEL = 75 LOAEL > 300 (RA)	No Data LOAEL = 300 (RA)
***p*-(alpha, alpha-Dimethylbenzyl)phenol or *p*-cumylphenol (CAS No. 599-64-4)**	**1770**	No Data > 2000 (RA)	No Data	No Data NOAEL = 100 LOAEL = 400 NOAEL = Not established LOAEL ~ 15 (RA)	No Data NOAEL = ~ 15 LOAEL = 650 (RA)	No Data NOAEL = 75 LOAEL > 300 (RA)	No Data LOAEL = 300 (RA)
***p*-Nonylphenol (CAS No. 84852-15-3)**	**1882**	No Data > 2000 (RA)	No Data	**NOAEL = 100 LOAEL = 400 NOAEL = Not established LOAEL ~ 15**	**NOAEL = ~ 15 LOAEL = 650**	**NOAEL = 75 LOAEL > 300**	**LOAEL = 300**
***p*-Dodecylphenol (CAS No. 210555-94-5)**	**2100**	No Data > 2000 (RA)	No Data	No Data NOAEL = 100 LOAEL = 400 NOAEL = Not established LOAEL ~ 15 (RA)	No Data NOAEL = ~ 15 LOAEL = 650 (RA)	No Data NOAEL = 75 LOAEL > 300 (RA)	No Data LOAEL = 300 (RA)

Di- and Tri-Substituted Mixed Alkylphenols							
2,3,6-Trimethylphenol (CAS No. 2416-94-6)	**>2000**	No Data > 1000 (RA)	No Data	No Data NOAEL = 15 LOAEL = 100 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)
2,4-Di-*tert*-butylphenol (CAS No. 96-76-4)	**1500**	No Data > 1000 (RA)	No Data	No Data NOAEL = 15 LOAEL = 100 (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**	No Data	**NOAEL = 15** **LOAEL = 100**	**NOAEL = 150** **LOAEL = 750**	**NOAEL = 150** **LOAEL = 750**	**NOAEL = 150** **LOAEL = 750**
2,4-Di-*tert*-pentylphenol (CAS No. 120-95-6)	**920**	No Data > 1000 (RA)	No Data	No Data NOAEL = 15 LOAEL = 100 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)
4-*sec*-Butyl-2,6-tert-butylphenol (CAS No. 17540-75-9)	**4800**	No Data > 1000 (RA)	No Data	No Data NOAEL = 15 LOAEL = 100 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)
2,4,6-Tri-*tert*-butylphenol (CAS No. 732-26-3)	**1670** **1610**	No Data > 1000 (RA)	No Data	**NOAEL ~ 1.5** **LOAEL ~ 5**	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)
2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 2772-45-4)	No Data (RA)	No Data > 1000 (RA)	No Data	No Data NOAEL ~ 1.5 LOAEL ~ 5 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)	No Data NOAEL = 150 LOAEL = 750 (RA)

Table 3. Summary of Human Health Data (Continued)

Chemical	Genetic Toxicity – Gene Mutation *In vitro*	Genetic Toxicity – Chromosomal Aberrations *In vitro*	Genetic Toxicity – Other Effects: Mouse Micronucleus (*in vivo*)	Irritation (skin)	Irritation (eye)
***o*-Substituted Alkylphenols**					
***o*-*sec*-Butylphenol (CAS No. 89-72-5)**	**Negative**	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
2-*tert*-Butylphenol (CAS No. 88-18-6)	**Negative**	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
***p*-Substituted Alkylphenols**					
***p*-*tert*-Butylphenol (CAS No. 98-54-4)**	**Negative**	**Negative**	—	Highly irritating or corrosive	Highly irritating or corrosive
***p*-*sec*-Butylphenol (CAS No. 99-71-8)**	**Negative**	**Negative**	—	Highly irritating or corrosive	Highly irritating or corrosive
***p*-*tert*-Amylphenol (CAS No. 80-46-6)**	**Negative**	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
Heptyl derivatives (*p*-heptylphenol) (CAS No. 72624-02-3)	**Negative**	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
***p*-*tert*-Octylphenol (CAS No. 140-66-9)**	**Negative**	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
***p*-Octylphenol (CAS No. 1806-26-4)**	No Data Negative (RA)	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
***p*-(alpha, alpha Dimethylbenzyl)-phenol or *p*-cumylphenol (CAS No. 599-64-4)**	**Negative**	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
***p*-Nonylphenol (CAS No. 84852-15-3)**	**Negative**	**Negative**	**Negative**	Highly irritating or corrosive	Highly irritating or corrosive
***p*-Dodecylphenol (CAS No. 210555-94-5)**	No Data Negative (RA)	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
Di- and Tri-Substituted Mixed Alkylphenols					
2,3,6-Trimethylphenol (CAS No. 2416-94-6)	**Negative**	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
2,4-Di-*tert*-butylphenol (CAS No. 96-76-4)	No Data Negative (RA)	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
2,6-Di-*tert*-butylphenol (CAS 128-39-2)	**Negative**	**Negative**	—	Highly irritating or corrosive	Highly irritating or corrosive

Table 3. Summary of Human Health Data (Continued)

Chemical	Genetic Toxicity – Gene Mutation *In vitro*	Genetic Toxicity – Chromosomal Aberrations *In vitro*	Genetic Toxicity – Other Effects: Mouse Micronucleus (*in vivo*)	Irritation (skin)	Irritation (eye)
2,4-Di-*tert*-pentylphenol (CAS No. 120-95-6)	No Data Negative (RA)	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
4-*sec*-Butyl-2,6-tert-butylphenol (CAS No. 17540-75-9)	**Negative**	**Negative**	—	Highly irritating or corrosive	Highly irritating or corrosive
2,4,6-Tri-*tert*-butylphenol (CAS No. 732-26-3)	No Data Negative (RA)	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive
2,4-bis(alpha, alpha-Dimethylbenzyl)phenol (CAS No. 2772-45-4)	No Data Negative (RA)	No Data Negative (RA)	—	Highly irritating or corrosive	Highly irritating or corrosive

bold – measured data; (RA) = Read Across

4. Hazard Characterization

The log K_{ow} of the members of the *o*-substituted alkylphenols subcategory indicates that their potential to bioaccumulate is expected to be low. The log K_{ow} of the members of the *p*-substituted alkylphenols subcategory with the smaller alkyl groups (butyl) indicates that their potential to bioaccumulate is expected to be low; the category members with the larger alkyl substituents have higher log K_{ow} values (mostly above 4) indicating their potential to bioaccumulate is expected to be high. The log K_{ow} of the di- and tri-substituted mixed alkylphenols subcategory members indicates that the potential to bioaccumulate is expected to be high.

o-Substituted alkylphenol subcategory members are not readily biodegradable, indicating that they have the potential to persist in the environment. Of the *p*-substituted alkylphenol subcategory members, *p-tert*-butylphenol and *p-sec*-butylphenol, are readily biodegradable, indicating that they do not have the potential to persist in the environment. All other *p*-substituted alkylphenol subcategory members are not readily biodegradable, indicating that they have the potential to persist in the environment. Di- and tri-substituted mixed alkylphenols subcategory members are not readily biodegradable, indicating that they have the potential to persist in the environment.

The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of *o*-substituted alkylphenols subcategory to aquatic organisms is moderate. The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of the majority of *p*-substituted alkylphenols subcategory to aquatic organisms is moderate. A few of the category members have high aquatic plant toxicity values, indicating that they may pose a high hazard to aquatic plants. The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of di- and tri-substituted mixed alkylphenols subcategory to aquatic organisms is moderate to high. Generally, the hazard potential for the category members with smaller substituents is moderate. Estimated toxicity values for category members with larger substituents indicate high potential hazard for fish and aquatic plants.

The acute oral toxicity for the members the alkylphenols category is low to moderate. Repeated exposures via the oral route of exposure resulted in effects on liver, kidney, testes and forestomach. Two- and three-generation reproduction toxicity studies indicate no treatment-related effects on reproductive or developmental endpoints,

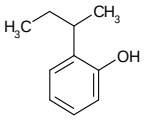
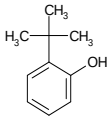
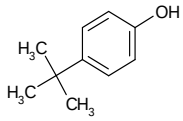
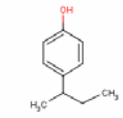
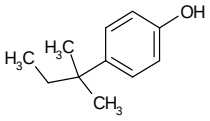
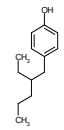
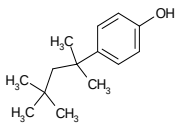
except body weight effects, in parents or offspring. No abnormalities in fetuses were reported for any members of the alkylphenol category. None of the category members showed mutagenic potential when tested in *Salmonella typhimurium.* No chromosomal aberrations were observed in cells tested with or without metabolic activation for any of the category members. When tested *in vivo* in a mouse micronucleus assay, *p*-nonylphenol did not induce cytogenetic damage. The category members are considered irritating to corrosive to the skin and irritating to eye.

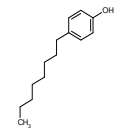
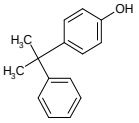
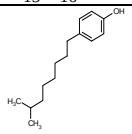
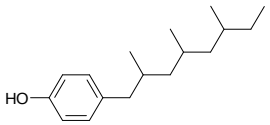
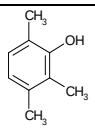
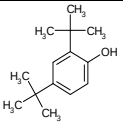
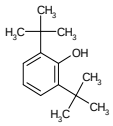
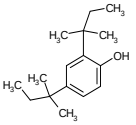
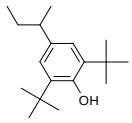
The potential health hazard of the alkylphenols category is moderate based on the limited data available for repeated-dose and reproductive toxicity.

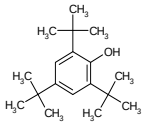
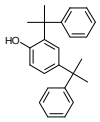
5. Data Gaps

No data gaps were identified under the HPV Challenge Program. All HPV Challenge Program endpoints have been adequately addressed by a combination of test data and read across from appropriate category chemicals where data gaps existed.

Appendix

Alkyphenols		
CAS No.	**Chemical Name**	**Structure**
SPONSORED CHEMICALS		
o-Substituted Alkylphenols		
89-72-5	***o-sec*-Butylphenol**	 $C_{10}H_{14}O$
88-18-6	**2-*tert*-Butylphenol**	 $C_{10}H_{14}O$
p-Substituted Alkylphenols		
98-54-4	***p-tert*-Butylphenol**	 $C_{10}H_{14}O$
99-71-8	***p-sec*-Butylphenol**	 $C_{10}H_{14}O$
80-46-6	***p-tert*-Amylphenol**	 $C_{11}H_{16}O$
72624-02-3	**Heptyl derivatives (*p*-heptylphenol)**	 Representative structure and formula; branching may vary
140-66-9	***p-tert*-Octylphenol**	 $C_{14}H_{22}O$

Alkyphenols		
CAS No.	**Chemical Name**	**Structure**
SPONSORED CHEMICALS		
1806-26-4	***p*-Octylphenol**	 $C_{14}H_{22}O$
599-64-4	***p*-(alpha, alpha-Dimethylbenzyl)phenol**	 $C_{15}H_{16}O$
84852-15-3	***p*-Nonylphenol**	 Representative structure; branching may vary
210555-94-5	***p*-Dodecylphenol**	 Representative structure; branching may vary
Di- and Tri-Substituted Mixed Alkylphenols		
2416-94-6	**2,3,6-Trimethylphenol**	 $C_9H_{12}O$
96-76-4	**2,4-Di-*tert*-butylphenol**	 $C_{14}H_{22}O$
128-39-2	**2,6-Di- *tert*-butylphenol**	 $C_{14}H_{22}O$
120-95-6	**2,4-Di-*tert*-pentylphenol**	 $C_{16}H_{26}O$
17540-75-9	**4-*sec*-Butyl-2,6-*tert*-butylphenol**	 $C_{18}H_{30}O$

Alkyphenols		
CAS No.	**Chemical Name**	**Structure**
SPONSORED CHEMICALS		
732-26-3	**2,4,6-Tri-*tert*-butylphenol**	 $C_{18}H_{30}O$
2772-45-4	**2,4-*bis*(alpha, alpha-Dimethylbenzyl)phenol**	 $C_{24}H_{26}O$