SCREENING-LEVEL HAZARD CHARACTERIZATION

Benzyl Derivatives Category

SPONSORED CHEMICALS
(See Section 1)

SUPPORTING CHEMICAL
Isoamyl Salicylate (CASRN 87-20-7)

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

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

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

OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and

[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. Risk Assessment Guidelines; http://cfpub.epa.gov/ncea/raf/rafguid.cfm.

Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

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

Chemical Abstract Service Registry Number (CASRN)	**<u>Sponsored Chemicals</u>** **100-52-7** **123-11-5** **121-33-5** **140-11-4** **120-51-4** **93-58-3** **99-75-2** **119-36-8** **2050-08-0** **118-58-1** **<u>Supporting Chemical</u>** **87-20-7**
Chemical Abstract Index Name	**<u>Sponsored Chemicals</u>** **Benzaldehyde** **Benzaldehyde, 4-methoxy** **Benzaldehyde, 4-hydroxy-3-methoxy** **Acetic acid, phenylmethyl ester** **Benzoic acid, phenylmethyl ester** **Benzoic acid, methyl ester** **Benzoic acid, 4-methyl-, methyl ester** **Benzoic acid, 2-hydroxy-, methyl ester** **Benzoic acid, 2-hydroxy-, pentyl ester** **Benzoic acid, 2-hydroxy-, phenylmethyl ester** **<u>Supporting Chemical</u>** **Benzoic acid, 2-hydroxy-, 3-methylbutyl ester**
Structural Formula	**See Section 1**

Summary

The benzyl derivatives category consists of liquid substances with the exception of CASRN 99-75-2, which is a colorless solid. The compounds in this category possess moderate vapor pressure and moderate to high water solubility. The substances in the benzyl derivatives category are expected to have moderate to high mobility in soil. Volatilization of the benzyl derivatives is considered moderate based on their Henry's Law constants. The rate of hydrolysis is considered negligible to slow for the members of this category. The rate of atmospheric photooxidation is considered moderate to negligible. The substances in the benzyl derivatives category are expected to have low persistence (P1) and low bioaccumulation potential (B1).

Human Health Hazard

Subcategory I: Benzaldehyde Derivatives

The acute oral toxicity of subcategory I members is low in rats and guinea pigs. The acute dermal toxicity of CASRN 100-52-7 is moderate in rabbits. In several National Toxicology Program (NTP) and other 13-week oral repeated-dose toxicity studies, CASRN 100-52-7 showed histopathological changes in various organ systems at 800 mg/kg/day in rats, and renal lesions and decreased body weight changes in male mice at 600 mg/kg/day. The NOAELs for systemic toxicity were 400 mg/kg/day and 300 mg/kg/day in rats and mice, respectively. No specific reproductive toxicity studies are available for CASRN 100-52-7; however, in the 13-week oral repeated-dose toxicity studies in rats and mice, no treatment related effects on reproductive organs were observed. CASRN 100-52-7 was not mutagenic in bacteria and mammalian cells *in vitro*. CASRN 100-52-7 induced chromosome aberrations in mammalian cells *in vitro* and was positive for sister chromatid exchanges in human lymphocytes *in vitro*. CASRN 100-52-7 did not induce unscheduled DNA synthesis in rat hepatocytes *in vitro*. CASRN 100-52-7 did not show an increased incidence of tumors in rats but showed an increase in the incidence of focal hyperplasia and squamous cell papillomas of the forestomach in mice.

The acute dermal toxicity of CASRN 123-11-5 is low in rabbits. The acute inhalation (vapor) toxicity of CASRN 123-11-5 in rats is high. In two oral repeated-dose toxicity studies with CASRN 123-11-5 in rats, no systemic effects were seen in rats; the NOAELs for systemic toxicity were 50 mg/kg/day (13 weeks; only dose tested) and 500 mg/kg/day (29-weeks; only dose tested). In a combined oral repeated-dose/reproductive/developmental toxicity screening test with CASRN 123-1-5, decreased body weights, decreased platelets and hypertrophy of hepatocytes were noted at 100 mg/kg/day; the NOAEL for systemic toxicity was 20 mg/kg/day. CASRN 123-11-5 showed significantly reduced fertility index, number of pups/litter, delivery index and number of live pups at 500 mg/kg/day; the NOAEL for reproductive/developmental toxicity was 100 mg/kg/day. CASRN 123-11-5 was not mutagenic in bacteria but mutagenic in mouse lymphoma cells *in vitro*. CASRN 123-11-5 induced chromosomal aberrations in Chinese Hamster Ovary (CHO) cells but not in fibroblast cells *in vitro*. CASRN 123-11-5 was positive for sister chromatid exchange in human lymph oocytes but not CHO cells *in vitro*.

In 16 to 28-week oral repeated-dose toxicity studies, CASRN 121-33-5 showed no treatment-related effects in rats and dogs; the NOAELs for systemic toxicity ranged from 50 (highest dose tested) to 500 mg/kg/day (only dose tested) in rats; the NOAEL for systemic toxicity for dogs was 100 mg/kg/day (highest dose tested). CASRN 121-33-5 was not mutagenic in bacteria and mouse lymphoma cells *in vitro*. CASRN 121-33-5 induced chromosomal aberrations in human lymphocytes but did not induce chromosomal aberrations in CHO cells and Chinese hamster fibroblasts *in vitro*. CASRN 121-33-5 induced sister chromatid exchanges in human lymphocytes but not in CHO cells *in vitro*. CASRN 121-33-5 did not induce unscheduled DNA synthesis in rat hepatocytes *in vitro*. CASRN 121-33-5 did not induce mouse micronuclei *in vivo*. CASRN 121-33-5 is irritating to rabbit and guinea pig skin.

No data gaps were identified under the HPV Challenge Program.

Subcategory II: Benzyl and Benzoate Esters

The acute oral toxicity of subcategory II members is low in rats, mice, rabbits, guinea pigs, and dogs. The acute inhalation toxicity of CASRN 93-58-3 is moderate in rats. The acute dermal toxicity of CASRN 120-51-4 in rats is low; and the acute dermal toxicity of CASRNs 93-58-3 and 99-75-2 in rabbits is low. In a 28-day repeated-dose toxicity study with CASRN 140-11-4, a significant decrease in body weight, absolute brain weight and mortality were seen in rats at 2000 mg/kg/day; the NOAEL for systemic toxicity was not established. Several NTP 13-week repeated-dose toxicity studies are available for rats and mice. Mice studies showed decreased final mean body weight and body weight gain, and relative and absolute organ weights in various organs of both sexes at 650 mg/kg/day (females) and 425 mg/kg/day (males); the NOAELs were not established for mice. Male rats showed testicular atrophy, decreased body weight gain, and mortality at dose ranges of 900 to 1000 mg/kg/day; the lowest rat NOAEL for systemic toxicity was 460 mg/kg/day. No specific reproductive toxicity studies are available; however, in the13-week dietary studies in rats and mice, no significant treatment related effects were observed on sperm morphology and vaginal cytology examinations. In an oral prenatal developmental toxicity study in rats, no maternal toxicity was seen. An increase in combined organ and skeletal variations were seen in the fetus at 500 mg/kg/day. The NOAEL for maternal and developmental toxicity was 1000 mg/kg/day (highest dose tested) and 100 mg/kg/day, respectively. CASRNs 120-51-4, 93-58-3 and 99-75-2 were not mutagenic in bacteria *in vitro*. CASRN 140-11-4 was mutagenic in human lymphoblasts and mouse lymphoma cells but not mutagenic in bacteria *in vitro*. CASRN 140-11-4 did not induce chromosomal aberrations or sister chromatid exchange in CHO cells *in vitro*. CASRN 140-11-4 did not induce mouse micronuclei *in vivo* or unscheduled DNA synthesis in rats *in vitro or in vivo*. Several two-year chronic/carcinogenicity studies were conducted with rats and mice by NTP. CASRN 140-11-4 showed evidence of pancreatic tumors in male rats. In the two-year study with rats and mice via oral gavage, CASRN 140-11-4 showed increased incidence of pancreatic acinar-cell adenomas in rats; hepatocellular adenomas and squamous cell neoplasms of the forestomach in mice. In two-year dietary studies in rats and mice, CASRN 140-11-4 showed no evidence of neoplasms in rats or mice.

No data gaps were identified under the HPV Challenge Program.

Subcategory III: 2-Hydroxybenzoate Esters
The acute oral toxicity of CASRN 119-36-8 is low in rats and mice. The acute oral toxicity of CASRN 118-58-1 is low in rats. The acute oral and dermal toxicity of CASRN 2050-08-0 is low in rats and rabbits, respectively. In an oral repeated-dose toxicity study with CASRN 2050-08-0 in rats, the LOAEL and NOAEL could not be established due to equivocal results for systemic toxicity in both sexes. In a 30-week dietary repeated-dose toxicity study in rats, decreased body weight gain was seen in both sexes at 315 (males) and 565 mg/kg/day (females); the NOAEL for systemic toxicity was 180 mg/kg/day and 315 mg/kg/day for males and females, respectively. A six-month oral repeated-dose toxicity study with CASRN 119-36-8 in dogs showed no adverse toxic effects; the NOAEL for systemic toxicity in dogs was 167 mg/kg/day (highest dose tested). However, dogs treated for two years by the same route, showed decreased growth and enlarged livers at 150 mg/kg/day; the NOAEL for systemic toxicity was 50 mg/kg/day. In two, three-generation dietary reproductive toxicity studies in rats with CASRN 119-36-8, no parental toxicity was observed up to 250 mg/kg/day (highest dose tested). In the first study, decrease in litter survival, and a decrease in average litter size and average number of live births per female was noted at 150 mg/kg/day; the NOAEL for reproductive/developmental toxicity was 75

mg/kg/day. In the second study, a decrease in mean number of litters, number of pups/litter, proportion of live births and mean live pup weights was observed at and above 500 mg/kg/day; the NOAEL for reproductive/developmental toxicity was 250 mg/kg/day. In a continuous breeding study in mice, CASRN 119-36-8 showed no treatment-related effects in adults up to 1000 mg/kg/day (highest dose tested) and decreased mean numbers of litters, number of pups/litter, proportion of live births and mean live pup weights at 1000 mg/kg/day; the NOAEL for reproductive/developmental toxicity was 500 mg/kg/day. CASRNs 119-36-8 and 118-58-1 were not mutagenic in bacteria *in vitro*. CASRN 119-36-8 did not induce chromosomal aberrations or sister chromatid exchange *in vitro*.

No data gaps were identified under the HPV Challenge Program.

Hazard to the Environment

Subcategory I: Aldehydes

The 96-h LC_{50} value for fish to CASRN 100-52-7 is 7.61 mg/L and to CASRN 123-11-5 is 40 mg/L. The 48-h EC_{50} for aquatic invertebrates to CASRN 123-11-5 is 45 mg/L. The 72-hr EC_{50} values for aquatic plants to CASRN 123-11-5 are 61 and 59 mg/L for growth rate and biomass, respectively.

No data gaps were identified under the HPV Challenge Program.

Subcategory II: Esters

The 96-h LC_{50} values for fish to CASRNs 140-11-4, 120-51-4 and 93-58-3 range from 1.34 to 28.3 mg/L. The 48-h EC_{50} value for aquatic invertebrates to CASRN 93-58-3 is 32.1 mg/L.

Toxicity to aquatic plants endpoint was identified as a data gap under the HPV Challenge Program.

Subcategory III: Ester/Phenols

The 96-h LC_{50} values for fish to CASRNs 2050-08-0 and 118-58-1 are 1.34 and 0.55 mg/L, respectively. The 48-hr EC_{50} value for aquatic invertebrates to CASRN 2050-08-0 is 2.8 mg/L.

Toxicity to aquatic plants and chronic toxicity to aquatic invertebrates endpoints were identified as data gaps under the HPV Challenge Program.

Subcategory IV: Aldehyde/Phenol

The 96-h LC_{50} value for fish to CASRN 121-33-5 is 53.0 mg/L.

Acute toxicity to aquatic invertebrates, and toxicity to aquatic plants endpoints were identified as data gaps under the HPV Challenge Program

The sponsor, The Flavor and Fragrance HPVC Aromatic Consortium, submitted a Test Plan and Robust Summaries to EPA for benzyl derivatives dated December 26, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on January 31, 2002 (http://www.epa.gov/oppt/chemrtk/pubs/summaries/benzylde/c13450tc.htm). EPA comments on the original submission were posted to the website on December 13, 2002. Public comments were also received and posted to the website.

Category Justification

The benzyl derivatives category includes 10 sponsored chemicals which contain a substituted or unsubstituted benzene ring bonded directly to a single oxygenated carbon. The sponsor provided pharmacokinetic data in support of a contention that the toxicologic properties of the category members should be similar based on the formation of similar stable metabolites (i.e., benzoic acid derivatives corresponding to the category members). All benzyl derivatives category members are structurally similar; however, the substituents and functional groups are different enough that the aldehydes, phenols and esters could each exhibit different toxicities and sensitivities. Based on the differences in the substituents, the chemicals are divided into the appropriate subcategories. For the purposes of hazard characterization, the chemicals are divided into three subcategories for human health.

For ecological effects, the combined effects of multiple functional groups on aquatic toxicity are unknown and because of the existence of different functional groups, the 10 sponsored chemicals are subdivided into four subcategories according to functional group structure consisting of (1) single aldehyde base structures (2 chemicals); (2) single ester base structures (four chemicals); (3) single ester and phenol base structures (3 chemiclas);and (4) single aldehyde and phenol base structures (1 chemical). EPA considers read-across between individual members within a particular subcategory to be appropriate for purposes of the HPV Challenge Program.

The CASRNs assigned to the subcategories are described in Table 1.

Justification for Supporting Chemical

Biodegradation data for isoamyl salicylate (CASRN 87-20-7) were provided in the robust summaries for the category member, pentyl-2-hydroxybenzoate (CASRN 2050-08-0). The sponsor did not provide justification for the use of this supporting chemical; however, the structural similarities of these two compounds make the use of isoamyl salicylate reasonable for the biodegradation of pentyl-2-hydroxybenzoate. EPA stated that the additional health effects studies provided by the sponsor for non-category members were too vague and their connection to the category members were not stated.

Table 1. Subcategories in the Benzyl Derivatives Category	
HUMAN HEALTH HAZARD	ECOTOXICITY
Subcategory I • CASRN 100-52-7 • CASRN 123-11-5 • CASRN 121-33-5	***Subcategory I*** • CASRN 100-52-7 • CASRN 123-11-5
Subcategory II • CASRN 140-11-4 • CASRN 120-51-4 • CASRN 93-58-3 • CASRN 99-75-2	***Subcategory II*** • CASRN 140-11-4 • CASRN 120-51-4 • CASRN 93-58-3 • CASRN 99-75-2
Subcategory III • CASRN 119-36-8 • CASRN 2050-08-0 • CASRN 118-58-1	***Subcategory III*** • CASRN 119-36-8 • CASRN 2050-08-0 • CASRN 118-58-1 • CASRN 87-20-7, *supporting chemical*
	Subcategory IV • CASRN 121-33-5

1. Chemical Identity

1.1 Identification and Purity

The following description is taken from the final Test Plan (2002):

The chemical category designated "Benzyl Derivatives" includes three benzaldehyde derivatives (benzaldehyde, *p*-methoxy, and *m*-methoxy-*p*-hydroxybenzaldehyde), two benzyl (benzyl acetate and benzyl benzoate) and two benzoate (methyl benzoate and methyl *p*-methylbenzoate) esters, and three 2-hydroxybenzoate esters (methyl, pentyl, and benzyl 2-hydroxybenzoate). The benzaldehyde derivatives are readily oxidized to the corresponding benzoic acid derivatives while the benzyl esters are hydrolyzed to yield benzyl alcohol that is subsequently oxidized to benzoic acid as a stable metabolite or end-product. The benzoate and 2-hydroxybenzoates esters are hydrolyzed to yield benzoic acid and 2-hydroxybenzoic acid derivatives, respectively. The 10 substances are placed in the same category because all contain a benzene ring bonded directly to an oxygenated functional group (aldehyde or ester) that is hydrolyzed and/or oxidized to a benzoic acid derivative. As a stable animal metabolite, benzoic acid derivatives are efficiently excreted primarily in the urine. These reaction pathways have been reported in both aquatic and terrestrial species. The similarity of their toxicologic properties is a reflection their participation in these common metabolic pathways.

This chemical category contains members that are some of the most widely used materials in flavors and fragrances and are widely distributed in the food supply. Some members of this category have common names derived from the foods in which they occur. Benzaldehyde is almost the exclusive constituent of bitter almond oil. *p*-Methoxybenzaldehyde and *m*-methoxy-

p-hydroxybenzaldehyde are commonly known as *p*-anisaldehyde and vanillin because of their presence in the spices, anise and vanilla, respectively. Of the esters in this category methyl 2-hydroxybenzoate or methyl salicylate is widely recognized as oil of wintergreen while the pentyl and benzyl 2-hydroxybenzoate are often called amyl salicylate and benzyl salicylate, respectively. Methyl *p*-methylbenzoate is often called methyl *p*-toluate.

The structures are provided in Table 2. Purity of the individual chemicals is specified in Section 3.

1.2 Physical-Chemical Properties

The physical-chemical properties of the substances contained in the benzyl derivatives category are summarized in Table 3.

The benzyl derivatives category consists of liquid substances with the exception of benzoic acid, 4-methyl-, methyl ester, which is a colorless solid. The compounds in this category possess moderate vapor pressure and moderate to high water solubility.

Table 2. Benzyl Derivatives Category

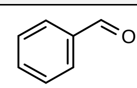
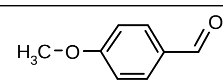
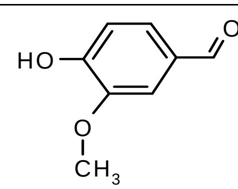
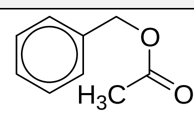
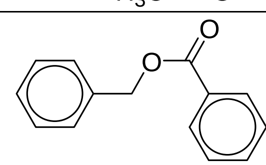
CASRN	Chemical Name	Chemical Structure
SPONSORED CHEMICALS		
Subcategory I: Benzyl Derivatives		
100-52-7	Benzaldehyde	
123-11-5	*p*-Methoxybenzaldehyde	
121-33-5	*m*-Methoxy-*p*-hydroxybenzaldehyde	
Subcategory II: Benzyl and Benzoate Esters		
140-11-4	Benzyl acetate	
120-51-4	Benzyl benzoate	

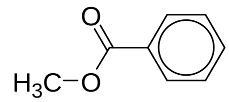
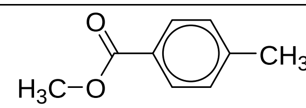
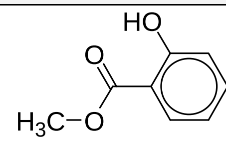
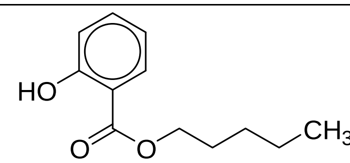
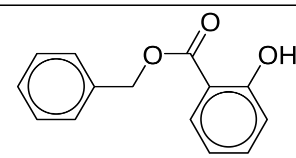
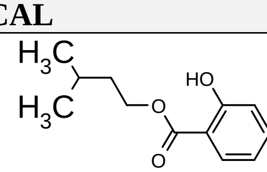
Table 2. Benzyl Derivatives Category		
CASRN	**Chemical Name**	**Chemical Structure**
93-58-3	Methyl benzoate	
99-75-2	Methyl *p*-methylbenzoate	
Subcategory III: 2-Hydroxybenzoate Esters		
119-36-8	Methyl-2-hydroxybenzoate	
2050-08-0	Pentyl-2-hydroxybenzoate	
118-58-1	Benzyl-2-hydroxybenzoate	
SUPPORTING CHEMICAL		
87-20-7	Isoamyl salicylate	

Table 3. Physical-Chemical Properties of Benzyl Derivatives Category[1]							
Property	**Benzoic acid, methyl ester**	**Benzoic acid, 4-methyl-, methyl ester**	**Benzoic acid, 2-hydroxy-, phenylmethyl ester**	**Benzoic acid, 2-hydroxy-, methyl ester**	**Benzoic acid, phenylmethyl ester**	**Acetic acid, phenylmethyl ester**	**Benzoic acid, 2-hydroxy-, pentyl ester**
CASRN	93-58-3	99-75-2	118-58-1	119-36-8	120-51-4	140-11-4	2050-08-0
Molecular Weight	136.15	150.18	228.25	152.15	212.25	150.18	208.26
Physical State	Liquid	Colorless solid	Liquid	Liquid	Liquid	Liquid	Liquid
Melting Point	-15 °C (measured); -12.4 °C (measured)	33.2-34.0 °C (measured)	24°C (measured)[2]	-8.6 °C (measured)	21 °C (measured)	-51 °C (measured)	6.5°C (measured)[3]; 2.6 °C (measured)
Boiling Point	198-200°C (measured)	220 °C (measured)	320 °C (measured)	220-224 °C (measured)	323-324 °C (measured)	213-216 °C (measured)	277-278 °C (measured)
Vapor Pressure	0.38 mm Hg at 25 °C (measured)	0.18 mm Hg at 25 °C (estimated)[4]	0.010 mm Hg at 20 °C (measured)	0.038 mm Hg at 25 °C (measured)	0.0010 mm Hg at 20 °C (measured); 0.00052 mm Hg at 25 °C (measured)	0.18 mm Hg at 25 °C (measured)	0.0085 mm Hg at 25 °C (estimated)[4]
Water Solubility	2,100 mg/L at 20 °C (measured)	425 mg/L at 25 °C (measured)[3]	143.5 mg/L at 25 °C (estimated)[5] I get 24.59 mg/L from EPI Suite	700 mg/L at 30 °C (measured)	34.8 mg/L at 25 °C (estimated)[5]	3,100 mg/L at 25 °C (measured)	41.4 mg/L at 25 °C (estimated)[5]
Dissociation Constant (pK_a)	Not applicable	Not applicable	9.82 (estimated)[6]	10.13 (estimated)[6]	Not applicable	Not applicable	9.82 (estimated)[6]
Henry's Law Constant	3.2×10^{-5} atm-m^3/mole	1.9×10^{-4} atm-m^3/mole	3.7×10^{-7} atm-m^3/mole	9.8×10^{-5} atm-m^3/mole	2.3×10^{-7} atm-m^3/mole	1.1×10^{-5} atm-m^3/mole	1.4×10^{-5} atm-m^3/mole

Table 3. Physical-Chemical Properties of Benzyl Derivatives Category[1]							
Property	**Benzoic acid, methyl ester**	**Benzoic acid, 4-methyl-, methyl ester**	**Benzoic acid, 2-hydroxy-, phenylmethyl ester**	**Benzoic acid, 2-hydroxy-, methyl ester**	**Benzoic acid, phenylmethyl ester**	**Acetic acid, phenylmethyl ester**	**Benzoic acid, 2-hydroxy-, pentyl ester**
	(estimated)[5]	(estimated)[5]	(estimated)[5]	(estimated)[5]	(estimated)[5]	(estimated)[5]	(estimated)[5]
Log K_{ow}	2.20 °C (measured)	2.70 (measured)	4.31 (estimated)	2.6 (measured)	3.97 (measured)	1.96 (measured)	4.57 (estimated)[5]

[1] The Flavor and Fragrance High Production Volume Consortia. The Aromatic Consortium. January 3, 2002. Test Plan and Robust Summary for the Benzyl Derivatives Category. Available online from: http://www.epa.gov/chemrtk/pubs/summaries/benzylde/c13450tc.htm. as of May 24, 2010.
[2] Lewis, R.J. Sr. ; Hawley's Condensed Chemical Dictionary, 13th Edition, New York, NY: John Wiley & Sons, Inc., p. 132, 1997.
[3] Beilstein Online database; searched May 28, 2002.
[4] NOMO5. 1987. Programs to Enhance PC-Gems Estimates of Physical Properties for Organic Compounds. The Mitre Corp.
[5] U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of March 24, 2010.
[6] SPARC; pKa/property server. Ver 4.5. Sept, 2009. Available at http://ibmlc2.chem.uga.edu/sparc/ as of May 10, 2010.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

The benzyl derivatives category chemicals had an aggregated production and/or import volume in the United States between 5.5 million pounds and 51.5 million pounds in calendar year 2005.

- CASRN 93-58-3: 1 to <10 million pounds;
- CASRN 99-75-2: 1 to <10 million pounds;
- CASRN 118-58-1: 500,000 to <1 million pounds;
- CASRN 119-36-8: 1 to <10 million pounds;
- CASRN 120-51-4: 1 to <10 million pounds;
- CASRN 140-11-4: 1 to <10 million pounds;
- CASRN 2050-08-0: <500,000 pounds;

CASRN 93-58-3:
Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include pesticide and other agricultural chemical manufacturing and resin and synthetic rubber manufacturing as intermediates; and synthetic dye and pigment manufacturing as coloring agents (dyes). No commercial and consumer uses were reported.

CASRN 99-75-2:
Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include resin and synthetic rubber manufacturing and synthetic dye and pigment manufacturing as intermediates. No commercial and consumer uses were reported.

CASRN 118-58-1:
No industrial processing and uses and commercial and consumer uses were reported.

CASRN 119-36-8:
Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include all other chemical product and preparation manufacturing; and all other food manufacturing. Non-confidential commercial and consumer uses of this chemical include "other."

CASRN 120-51-4:
Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing as odor agents. Non-confidential commercial and consumer uses of this chemical include not readily obtainable (NRO) and "other."

CASRN 140-11-4:
Industrial processing and uses for the chemical were claimed confidential. Non-confidential commercial and consumer uses of this chemical include "other."

CASRN 2050-08-0:
No industrial processing and uses and commercial and consumer uses were reported.

2.2 Environmental Exposure and Fate

The environmental fate properties are provided in Table 4.

The substances in the benzyl derivatives category are expected to have moderate to high mobility in soil. Benzoic acid, methyl ester; benzoic acid, phenylmethyl ester; and acetic acid, phenylmethyl ester were all readily biodegradable achieving greater than 90% biodegradation during a 28 day incubation period as measured by CO_2 evolution using the modified Sturm test (OECD 301B). Benzoic acid, 2-hydroxy-, phenylmethyl ester degraded 87% after 28 days using the manometric respirometry test (OECD 301F) and was considered readily biodegradable. Benzoic acid, 2-hydroxy-, methyl ester degraded over 98% within a 28 day incubation period using a sealed vessel CO_2 production test (OPPTS 835.3120). A structural isomer to benzoic acid, 2-hydroxy-, pentyl ester (benzoic acid, 2-hydroxy-, 3-methylbutyl ester, CASRN 87-20-7) was readily biodegradable using the manometric respirometry test (OECD 301F). Volatilization of the benzyl derivatives is considered moderate based on their Henry's Law constants. The rate of hydrolysis is considered negligible to slow for all members of the category. The substances in the benzyl derivatives category are expected to have low persistence (P1) and low bioaccumulation potential (B1).

Table 4. Environmental Fate Characteristics of Benzyl Derivatives Category[1]							
Property	**Benzoic acid, methyl ester**	**Benzoic acid, 4-methyl-, methyl ester**	**Benzoic acid, 2-hydroxy-, phenylmethyl ester**	**Benzoic acid, 2-hydroxy-, methyl ester**	**Benzoic acid, phenylmethyl ester**	**Acetic acid, phenylmethyl ester**	**Benzoic acid, 2-hydroxy-, pentyl ester**
CASRN	93-58-3	99-75-2	118-58-1	119-36-8	120-51-4	140-11-4	2050-08-0
Photo-degradation Half-life	12.7 days (estimated)[2]	5.4 days (estimated)[2]	7.4 hours (estimated)[2]	11.6 hours (estimated)[2]	18.4 hours (estimated)[2]	20.1 hours (estimated)[2]	7.6 hours (estimated)[2]
Hydrolysis Half-life	5.5 years at pH 7 (estimated)[2]; 201 days at pH 8 (estimated)[2]	10.8 years at pH 7 (estimated)[2]; 1.1 years at pH 8 (estimated)[2]	1.7 years at pH 7 (estimated)[2]; 63 days at pH 8 (estimated)[2]	5.5 years at pH 7 (estimated)[2]; 201 days at pH 8 (estimated)[2]	1.7 years at pH 7 (estimated)[2]; 63 days at pH 8 (estimated)[2]	198 days at pH 7 (estimated)[2]; 19.8 days at pH 8 (estimated)[2]	6.9 years at pH 7 (estimated)[2]; 250 days at pH 8 (estimated)[2]
Biodegradation	95.3% after 28 days (readily biodegradable)	No data	87% after 28 days (readily biodegradable)	98.4% in 28 days (readily biodegradable)	93% in 28 days (readily biodegradable)	100% in 28 days (readily biodegradable)	29% in 28 days (not readily biodegradable)[1,3]; 84% in 28 days (readily biodegradable)[1,3]
Bioaccumulation Factor	BAF = 7.1 (estimated)[2]	BAF = 29.9 (estimated)[2]	BAF = 16.6 (estimated)[2]	BAF = 9.2 (estimated)[2]	BAF = 19.5 (estimated)[2]	BAF = 3.0 (estimated)[2]	BAF = 55.0 (estimated)[2]
Log K_{oc}	1.8 (estimated)[2]	2.0 (estimated)[2]	3.5 (estimated)[2]	1.9 (estimated)[2]	3.4 (estimated)[2]	2.1 (estimated)[2]	3.0 (estimated)[2]
Fugacity (Level III Model)[2]							
Air (%)	7.1	5.1	1.0	3.0	1.4	2.9	1.3
Water (%)	27.5	26.5	22.5	26.5	20.8	26.9	23.9
Soil (%)	65.2	68.3	74.2	70.4	76.1	70.0	73.9
Sediment (%)	0.1	0.2	2.3	0.1	1.7	0.2	0.8
Persistence[4]	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)

Table 4. Environmental Fate Characteristics of Benzyl Derivatives Category[1]

Property	**Benzoic acid, methyl ester**	**Benzoic acid, 4-methyl-, methyl ester**	**Benzoic acid, 2-hydroxy-, phenylmethyl ester**	**Benzoic acid, 2-hydroxy-, methyl ester**	**Benzoic acid, phenylmethyl ester**	**Acetic acid, phenylmethyl ester**	**Benzoic acid, 2-hydroxy-, pentyl ester**
Bioaccumulation[4]	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)

[1] The Flavor and Fragrance High Production Volume Consortia. The Aromatic Consortium. January 3, 2002. Test Plan and Robust Summary for the Benzyl Derivatives Category. Available online from: http://www.epa.gov/chemrtk/pubs/summaries/benzylde/c13450tc.htm. as of May 24, 2010.
[2] U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of March 24, 2010.
[3] Data obtained for a structurally related isomer benzoic acid, 2-hydroxy-, 3-methylbutyl ester (CASRN 87-20-7)
[4] Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

Conclusions: The benzyl derivatives category consists of liquid substances with the exception of benzoic acid, 4-methyl-, methyl ester, which is a colorless solid. The compounds in this category possess moderate vapor pressure and moderate to high water solubility. The substances in the benzyl derivatives category are expected to have moderate to high mobility in soil. Volatilization of the benzyl derivatives is considered moderate based on their Henry's Law constants. The rate of hydrolysis is considered negligible to slow for the members of this category. The rate of atmospheric photooxidation is considered moderate to negligible. The substances in the benzyl derivatives category are expected to have low persistence (P1) and low bioaccumulation potential (B1).

3. Human Health Hazard

A summary of health effects data submitted for SIDS endpoints is provided in Table 5. For CASRNs 100-52-7 and 121-33-5, the SIARs and Dossiers were finalized and published by the UNEP at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf, and http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf For CASRN 123-11-5, the draft SIAP is available at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0; no SIAR/IUCLID has been completed (SIAM 29) in 2009.

Acute Oral Toxicity

Subcategory I: Benzaldehyde Derivatives
Benzaldehyde (CASRN 100-52-7)
(1) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
LD_{50} = 1300 mg/kg

(2) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
LD_{50} = 1000 mg/kg

p-Methoxybenzaldehyde (CASRN 123-11-5)
(1) See human health data at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
LD_{50} = 1510 mg/kg

(2) See human health data at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
LD_{50} > 2000 mg/kg

m-Methoxy-p-hydroxybenzaldehyde (CASRN 121-33-5)
(1) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
LD_{50} = 1580 mg/kg

(2) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
LD_{50} = 1400 mg/kg

Subcategory II: Benzyl and Benzoate Esters
Benzyl acetate (CASRN 140-11-4)
(1) Osborne-Mendel rats (5/sex/dose) were fasted 18 hours before treatment and then administered benzyl acetate via oral gavage at unspecified doses and observed for 2 weeks following dosing. The number of deaths at each dose level was not reported. Deaths occurred between 4 hours and 3 days of treatments.
LD_{50} = 2490 mg/kg

(2) Thirty rats (strain and sex not provided, at least 5/dose) were administered benzyl acetate via oral gavage at unspecified doses and observed for the following 2 weeks.
LD_{50} = 3690 mg/kg

(3) In a National Toxicology Program (NTP) study, F344/N rats and B6C3F1 mice (5/sex/dose) were administered benzyl acetate via oral gavage (in corn oil) at 250, 500, 1000, 2000 or 4000 mg/kg, followed by a 15-day observation period. At 4000 mg/kg, 4/5 male rats and 2/5 female rats died on day two. LD_{50} values were not calculated, but are estimated to be > 2000 < 4000 mg/kg for rats and mice.
LD_{50} > 2000 mg/kg < 4000 mg/kg

Benzyl benzoate (CASRN 120-51-4)
(1) Rats, mice, rabbits and guinea pigs (10/species; sex not specified) were administered benzyl benzoate via oral gavage at a total of 2.0 mg/kg. All study information was not provided. LD_{50} values were calculated from the dose-mortality curve and ranged from 1.0 to 1.8 mL/kg (~ 1100 – 1980 mg/kg for all species.
LD_{50} ~ 1100 – 1980 mg/kg

(2) Rats (5/dose; strain and sex not specified) were fasted for 24 to 48 hours and later administered benzyl benzoate via oral gavage at unspecified doses, and were observed for two weeks or until death. The number of deaths at each dose level was not reported.
LD_{50} = 2800 mg/kg

(3) Rabbits (3/dose; strain and sex not specified) were fasted for 24 to 48 hours and later administered benzyl benzoate via oral gavage at unspecified doses, and were observed for 2 weeks or until death. The number of deaths at each dose level was not reported.
LD_{50} = 1680 mg/kg

(4) Four dogs (sex and strain specified) were fasted for 24 to 48 hours and later administered benzyl benzoate via oral gavage at doses up to 22,440 mg/kg, followed by a 2-week observation period. The number of deaths at each dose level was not reported.
LD_{50} > 22,440 mg/kg

Methyl benzoate (CASRN 93-58-3)
(1) Male Wistar rats (5/dose) were administered methyl benzoate via oral gavage at a single unspecified dose, followed by a 14-day observation period. The number of deaths at each dose level was not reported.
LD_{50} = 3430 mg/kg

(2) Rats (24/dose; strain and sex not specified) were administered methyl benzoate via oral gavage at 1000, 2000, 3000, 4000 or 5000 mg/kg, followed by a 14-day observation period. Animals that were given 5000 mg/kg died within 2 to three hours of administration. Animals that were given 4000 mg/kg died within 14 days of administration.
LD_{50} = 3500 mg/kg

(3) Rats (5/dose; strain and sex not specified) were fasted for 24 to 48 hours and later administered methyl benzoate via oral gavage at unspecified doses, followed by 2 weeks of observation. The number of deaths at each dose level was not reported.
LD_{50} = 2170 mg/kg

(4) White mice (20/dose; strain and sex not specified) were administered methyl benzoate via gavage at 500, 1000, 2000, 3000, 3500 or 4000 mg/kg, followed by a 14-day observation period. The number of deaths at each dose level was not reported.
LD_{50} = 3000 mg/kg

Methyl p-methylbenzoate (CASRN 99-75-2)
Rats (10/dose; strain and sex not provided) were administered methyl *p*-methylbenzoate via an unspecified oral route at 1220, 1730, 2470 or 5000 mg/kg/day. Mortalities occurred at 1/10 at 1730, 2/10 at 2470 and 10/10 at 5000 mg/kg.
LD_{50} = 3300 mg/kg

Subcategory III: 2-Hydroxybenzoate Esters
Methyl 2-hydroxybenzoate (CASRN 119-36-8)
(1) Male ddY mice (number per dose not provided) were administered methyl 2-hydroxybenzoate via oral gavage at 1000, 1200, 1300, 1500 or 1700 mg/kg, followed by a 7-day observation period. Mortalities occurred at all dose levels. The number of deaths at each dose level was not reported.
LD_{50} = 1390 mg/kg

(2) Osborne-Mendel rats (5/sex/dose) were administered methyl 2-hydroxybenzoate via oral gavage at unspecified doses, followed by observation for up to 2 weeks. Mortality was not reported.
LD_{50} = 887 mg/kg/day

(3) Sprague-Dawley rats (5/sex/dose) were administered methyl 2-hydroxybenzoate via oral gavage at 2500, 3150, 3969 or 5001 mg/kg, followed by observation for 14 days. Mortalities were noted for all dose levels.
LD_{50} = 2642 mg/kg

Pentyl 2-hydroxybenzoate (CASRN 2050-08-0)
(1) Rats (10/dose; strain and sex not specified) were administered pentyl 2-hydroxybenzoate via oral gavage (method unspecified) at 0, 3100, 4000, 5000 or 6300 mg/kg. Observation period following administration was unspecified. Mortality was observed at 3100(4), 4000(4), 5000(7), and 6300(10) mg/kg.
LD_{50} = 4100 mg/kg

(2) Sprague-Dawley rats (5/sex/dose) were administered a single dose of pentyl 2-hydroxybenzoate at 5000 mg/kg, followed by a 14-day observation period. No deaths were observed.
LD_{50} > 5000 mg/kg

Benzyl 2-hydroxybenzoate (CASRN 118-58-1)
Male rats (6/dose; strain unspecified) were administered a single dose of benzyl 2-hydroxybenzoate via oral gavage at 0, 1250, 2500 or 5000 mg/kg and observed for seven days. Mortality was observed at 2500(4) and 5000(6) mg/kg.
LD_{50} = 2227 mg/kg

Acute Inhalation Toxicity

Subcategory I: Benzaldehyde Derivatives
p-Methoxybenzaldehyde (CASRN 123-11-5)
See human health data at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
LC_{50} = 0.32 mg/L

Subcategory II: Benzyl and Benzoate Esters
Methyl benzoate (CASRN 93-58-3)
Carworth-Wistar rats (6/concentration; sex not specified) were exposed to saturated atmospheres of methyl benzoate for 8 hours, followed by a 14-day observation period. Nominal concentrations were increased by 2 logarithmic orders. No mortalities were seen at any exposure level. The LC_{50} was noted as > 1000 ppm (5.57 mg/L).
LC_{50} > 5.57 mg/L

Acute Dermal Toxicity

Subcategory I: Benzaldehyde Derivatives
Benzaldehyde (CASRN 100-52-7)
See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
LD_{50} > 1250 mg/kg

p-Methoxybenzaldehyde (CASRN 123-11-5)
See human health data at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
LD_{50} > 5000 mg/kg

Subcategory II: Benzyl and Benzoate Esters
Benzyl benzoate (CASRN 120-51-4)
Rats (number, dose, sex and strain not specified) were administered benzyl benzoate via the dermal route (conditions unspecified). No additional study details or results were provided. The LD_{50} was calculated based on a dose-mortality curve.
LD_{50} ~ 4400 mg/kg

Methyl benzoate (CASRN 93-58-3)
New Zealand White rabbits (5/sex/dose) were administered a single dose of methyl benzoate via the dermal route at 2000 mg/kg (conditions unspecified), followed by a 14-day observation period.
LD_{50} > 2000 mg/kg

Methyl p-methylbenzoate (CASRN 99-75-2)
Rabbits (10/dose; strain and sex not provided) were administered methyl *p*-methylbenzoate via the dermal route at 5000 mg/kg under unspecified conditions. No mortalities were noted.
LD_{50} > 5000 mg/kg

Subcategory III: 2-Hydroxybenzoate Esters
Pentyl 2-hydroxybenzoate (CASRN 2050-08-0)
Rabbits (10/dose; strain and sex unspecified) were administered a single dose of pentyl 2-hydroxybenzoate via the dermal route at 5000 mg/kg (site preparation and conditions unspecified). No mortalities were reported.
LD_{50} > 5000 mg/kg

Repeated-Dose Toxicity

Subcategory I: Benzaldehyde Derivatives
Benzaldehyde (CASRN 100-52-7)
(1) In a 16-week feeding study, Osborne-Mendel rats (5/sex/dose) were fed 10,000 ppm test substance via the diet. No adverse effects reported. See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
NOAEL ~ 500 mg/kg/day (highest dose tested)

(2) In a 27-28 week feeding study, Osborne-Mendel rats (5/sex/dose) were fed 1000 ppm test substance in the diet. No adverse effects reported. See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
NOAEL ~ 50 mg/kg/day (highest dose tested)

(3) In a 13-week National Toxicology Program (NTP) study, F344/N rats were administered 0, 50, 100, 200, 400 or 800 mg/kg/day test substance by oral gavage daily. Mortality, multiple histopathologic effects and decreased body weights were observed at 800 mg/kg/day. See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
LOAEL = 800 mg/kg/day (based on mortality, histopathological effects in brain, forestomach, liver and kidneys)
NOAEL = 400 mg/kg/day

(4) In a 13-week NTP study, B6C3F1 mice (10/sex/dose) were administered 0, 75, 150, 300 or 600 mg/kg/day test substance by oral gavage. Mortality was observed at the highest dose. Renal tubul degeneration occurred in all males. See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
LOAEL = 600 mg/kg/day (based on based on mortality)
NOAEL = 300 mg/kg/day

(5) In a two-year NTP study, F344 rats (50/sex/dose) were administered 0, 200 or 400 mg/kg/day test substance by oral gavage daily. Survival was significantly decreased in high-dose males. See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
LOAEL = 400 mg/kg/day (based on mortality in male rats)
NOAEL = 200 mg/kg/day

p-Methoxybenzaldehyde (CASRN 123-11-5)
(1) In a combined repeated-dose/reproductive/developmental toxicity screening test Crj:CD (SD)IGS rats (13/sex/dose) were given *p*-methoxybenzaldehyde at a dose of 0 (vehicle: corn oil), 20, 100 or 500 mg/kg/day. Males were dosed for 42 days from day 14 before mating and females were dosed for day 14 before mating, during mating (males and females), gestation periods to day 4 of lactation (females). No animals died in any group. Temporary salivation after administration was observed in males and females at 500 mg/kg/day. Body weights tended to be increased in males in the 500 mg/kg/day group and in females of the 100 and 500 mg/kg/day groups. A decrease in platelets was observed in males at 500 mg/kg/day and in females at 100 and 500 mg/kg/day. On biochemical analysis, the A/G ratio, GOT activity and inorganic phosphorus concentration were increased in males at 500 mg/kg/day. Hyperplasia of squamous count epithelium in the forestomach was detected in males and females at 100 and 500 mg/kg/day. At 500 mg/kg/day, the liver weight was increased in males and females. Histopathological examinations showed centrilobular hypertrophy of hepatocytes in these animals. See human health data at
http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
LOAEL (systemic toxicity) = 100 mg/kg/day (based on decreased body weight, decreased platelets and hypertrophy of hepatocytes)
NOAEL (systemic toxicity) = 20 mg/kg/day

(2) See human health data at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=624478ca-b163-434a-8b6c-bae2cfa08e0c&idx=0
NOAEL (systemic toxicity) ~ 500 mg/kg/day (only dose tested).

(3) See human health data at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
NOAEL (systemic toxicity) ~ 50 mg/kg/day (only dose tested).

m-Methoxy-p-hydroxybenzaldehyde (CASRN 121-33-5)
(1) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
In a 16-week study, Osborne-Mendel rats were exposed to 10,000 ppm test substance via the diet.
NOAEL (systemic toxicity) ~ 500 mg/kg/day (only dose tested)

(2) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
In a 27-week study, Osborne-Mendel rats were exposed to 1000 ppm test substance via the diet.
NOAEL (systemic toxicity) ~ 50 mg/kg/day (highest dose tested)

(3) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
In a 26-week feeding study, male albino rats (10/dose) were administered 0. 0.1, 0.5 or 1.0% (approximately 0, 40, 214 or 437 mg/kg/day) test substance ad libitum. There were no significant differences in survival, body weight, food consumption and pathology between treated and control animals.
NOAEL (systemic toxicity) ~ 437 mg/kg/day (highest dose tested)

(4) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
In a 26-27 week study dogs were exposed to 0, 25 or 100 mg/kg/day test substance via orally administered capsules.
NOAEL (systemic toxicity) = 100 mg/kg/day (highest dose tested)

(5) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
Mice (S-strain) were applied 3000 mg/kg-bw test substance dermally for a total of ten applications and observed for 18 weeks. No incidence of tumors of the lung.
NOAEL ~ 3000 mg/kg/day (highest dose tested)

Subcategory II: Benzyl and Benzoate Esters
Benzyl acetate (CASRN 140-11-4)
(1) F344 male rats (35/dose) were administered benzyl acetate in the diet at 0, 20,000, 35,000 or 50,000 ppm (approximately 0, 2000, 3500 or 5000 mg/kg/day) for 28 days. A functional observational battery (FOB) test, histopathology and immunochemistry were conducted. Mortality rates were 4/35 and 35/35 (died by day 12) at 3500 and 5,000 mg/kg/day respectively. These treated animals, at the two highest concentrations, exhibited ataxia, convulsions, neuronal necrosis in the brain and lesions in the skeletal muscle, liver and kidneys. A dose-related decrease in body weight was noted in all treated animals. A significant decrease in body weight gain were seen at 3500 and 5000 mg/kg/day along with a significant decrease in absolute brain weights. At 3500 mg/kg/day, a significant increase in relative body weights to brain weights was observed.
LOAEL (systemic toxicity) ~ 2000 mg/kg/day (based on decreased body weights)
NOAEL (systemic toxicity) = Not established

(2) F344 rats (10/sex/dose) were administered benzyl acetate in the diet at 0, 3130, 6250, 12,500, 25,000 or 50,000 ppm (~ 0, 230, 460, 900, 1750 or 3900 mg/kg/day for males and ~ 0, 240, 480, 930, 1870 or 4500 mg/kg/day for females) in a 13-week NTP study. The mortality rate for all animals at the highest concentration was 9/10 (90%). One female at 930 mg/kg/day died during week 10. Survival at all other concentrations was 100%. Final body weights and overall body weight gains were significantly decreased at 1750 mg/kg/day ($p < 0.01$ for males) and 930 mg/kg/day ($p < 0.05$ for females). At the highest concentration, relative and absolute weights of the brain, thymus, kidneys and uterus were slightly decreased in both sexes. At the same dose, histopathological examinations revealed brain necrosis (involving the cerebellum and/or hippocampus), renal tubule degeneration and regeneration, degeneration and hyperplasia of the tongue and skeletal muscles in both sexes. The cholesterol levels of females receiving 930 mg/kg/day and 4500 mg/kg/day were decreased, but there were no other changes noted in clinical chemistry parameters for treated males or females. Testicular atrophy was seen in two males at 1750 mg/kg/day and one male at 900 mg/kg/day.

LOAEL (systemic toxicity$_{(f)}$) ~ 930 mg/kg/day (based on decreased body weight gain, decreased cholesterol levels)
NOAEL (systemic toxicity$_{(f)}$) ~ 480 mg/kg/day
LOAEL (systemic toxicity$_{(m)}$) ~ 900 mg/kg/day (based on testicular atrophy)
NOAEL (systemic toxicity$_{(m)}$) ~ 460 mg/kg/day

(3) In an NTP study, F344 rats (10/sex/dose) were administered benzyl acetate (96% purity) in corn oil via oral gavage at 62.5, 125, 250, 500 or 1000 mg/kg/day, 5 days/week for 13 weeks. Histopathological examinations were conducted on controls and 1000 mg/kg/day treatment groups with at least 60% survival and animals that died before study termination. Mortalities (2/10 males, 1/10 females) were noted at 1000 mg/kg/day and the final mean body weight of the males in this group was 12% lower than controls. Clinical signs observed in males at 1000 mg/kg/day and females at 1000 and 500 mg/kg/day included ataxia, trembling and sluggishness. Necropsy revealed thickened stomach walls in 2/9 males and 4/10 females at 1000 mg/kg/day. No additional histopathological changes were noted.
LOAEL (systemic toxicity) = 1000 mg/kg/day (based on mortality, decreased body weights, thickened stomach walls)
NOAEL (systemic toxicity) = 500 mg/kg/day)

(4) In an NTP study, B6C3F1 mice (10/sex/dose) were administered benzyl acetate in the diet at 0, 3130, 6250, 12,500, 25,000 or 50,000 ppm (approximately 0, 425, 1000, 2000, 3700 or 7900 mg/kg/day for males and 0, 650, 1280, 2980, 4300 or 9400 mg/kg/day for females) for 13 weeks. One male and one female died at the highest dose. Females exhibited tremors at 2980, 4300, and 9400 mg/kg/day. All treated animals exhibited decreased final mean body weights and mean body weight gains along with differences in relative and absolute weights of the brain, kidney, liver, pancreas, prostate, seminal vesicle, spleen, testis and thymus. Hematology and clinical chemistry parameters were not affected in either sex. Histopathological examinations revealed liver and brain necrosis in four females at 9400 mg/kg/day and one male at 7900 mg/kg/day.
LOAEL (systemic toxicity$_{(f)}$) ~ 650 mg/kg/day (based on decreased final mean body weights and body weight gain, relative and absolute organ weights in various organs)
NOAEL (systemic toxicity$_{(f)}$) ~ Not Established
LOAEL (systemic toxicity$_{(m)}$) ~ 425 mg/kg/day (based on decreased final mean body weights and body weight gain, relative and absolute organ weights in various organs)
NOAEL (systemic toxicity$_{(m)}$) ~ Not Established

(5) In an NTP study, B6C3F1 mice (10/sex/dose) were administered benzyl acetate via gavage at 62.5, 125, 250, 500 or 1000 mg/kg/day (males) and 0, 125, 250, 500, 1000 or 2000 mg/kg/day (females), 5 days/week for 13 weeks. At 2000 mg/kg/day, female mice exhibited trembling, inactivity, labored breathing, depressed body temperature and death (8/10; one death was due to gavage error). There was no treatment-related mortality in males and no gross or pathological changes were observed in any mice.
LOAEL (systemic toxicity$_{(f)}$) = 2000 mg/kg/day (mortality)
NOAEL (systemic toxicity$_{(f)}$) = 1000 mg/kg/day
NOAEL (systemic toxicity$_{(m)}$) = 1000 mg/kg/day (highest dose tested**)**

Subcategory III: 2-Hydroxybenzoate Esters
Methyl 2-hydroxybenzoate (CASRN 119-36-8)
(1) In a 17-week study, Osborne-Mendel rats (10/sex/dose) were administered methyl 2-hydroxybenzoate in the diet at 0, 0.1 or 1.0% (approximately 0, 50 or 500 mg/kg/day). No mortalities or toxic effects were noted at any concentration. Body weight gain was reduced in rats receiving 1.0%. Liver, kidney, spleen and testes weights were unaffected by treatment and microscopic examination of these organs from four males and four females from the control and 1% groups each revealed no treatment-related effects.
LOAEL (systemic toxicity) ~ 500 mg/kg/day (based on reduced body weight gain)
NOAEL (systemic toxicity) ~ 50 mg/kg/day

(2) In a 30-week study, Sprague-Dawley rats (5/sex/dose) were administered methyl 2-hydroxybenzoate in the diet at 0, 0.2, 0.36, 0.63, 1.13 or 2.0% (approximately 0, 100, 180, 315, 565 or 1000 mg/kg/day). Decreased body weight gain and food consumption were noted in male rats at 315, 565, and 1000 mg/kg/day and in female rats at 565 and 1000 mg/kg/day. At 10 weeks, x-rays revealed increased bone density in the growth areas of the femur, tibia, humerus and radius in rats at 565 and 1000 mg/kg/day. However, significance of this finding is unclear.
LOAEL (systemic toxicity$_{(m)}$) ~ 315 mg/kg/day (based on decreased body weight gain)
NOAEL (systemic toxicity$_{(m)}$) ~ 180 mg/kg/day
LOAEL (systemic toxicity$_{(f)}$) ~ 565 mg/kg/day (based on decreased body weight gain)
NOAEL (systemic toxicity$_{(f)}$) ~ 315 (females) mg/kg/day

(3) In a six-month study, beagle dogs (4 – 6/sex/dose) were administered methyl 2-hydroxybenzoate via capsule at 0, 50, 100 or 167 mg/kg/day in two divided doses. Treatment was discontinued for two males and two females from the control and high-dose groups at 6 months; these animals were maintained on base diet for an additional 2 months. No mortalities occurred at any dose level. Hematological analysis was comparable between all treated dogs and the controls. Necropsy and histological examination of the liver and kidneys revealed no difference between the treated dogs and controls.
NOAEL (systemic toxicity) = 167mg/kg/day (highest dose tested)

(4) In a two-year study, beagle dogs (2/sex/dose) were administered methyl 2-hydroxybenzoate via capsule at 0, 50, 150 or 350 mg/kg/day, 6 days/week. Hematology was conducted periodically throughout the study. No mortalities or clinical signs of toxicity were noted. At the two highest doses, dogs exhibited decreased growth and enlarged livers. No other effects on hematology parameters or histopathology of high-dose dogs. No treatment-related effects were seen in the 50 mg/kg/day dose group.
LOAEL (systemic toxicity) = 150 mg/kg/day (based on decreased growth and enlarged livers)
NOAEL (systemic toxicity) = 50 mg/kg/day

(5) In a two-year study, Osborne-Mendel rats (25/sex/dose) were administered methyl 2-hydroxybenzoate in the diet at 0, 0.1, 0.5, 1 or 2% (approximately 0, 50, 250, 500 or 1000 mg/kg/day). Mortality was 100% in the highest dose group with no survival past day 49. These rats exhibited increased amounts of cancellous bone tissue and decreased numbers of osteoclasts compared to controls. A slight increase in cancellous bone tissue was also observed in one and two rats at 250 and 500 mg/kg/day, respectively. Inhibited growth was noted for rats at 500 and

1000mg/kg/day. No other treatment-related changes were noted for hematological parameters, organ weights or upon gross and microscopic examination of tissues from thyroid, parathyroid, lung, heart, stomach, pancreas, spleen, liver, kidney, adrenal, lymph node, small intestine, bone marrow, muscle, urinary bladder and testis and prostate or ovary and uterus.
LOAEL (systemic toxicity) ~500 mg/kg/day (based on decreased growth)
NOAEL (systemic toxicity) ~250 mg/kg/day

Pentyl 2-hydroxybenzoate (CASRN 2050-08-0)
Wister rats (15/sex/dose) were administered pentyl 2-hydroxybenzoate in the diet at 0, 4.7, 46, and 415 mg/kg/day for males and 0, 4.8, 46.9, and 475 mg/kg/day for females for 13 weeks. No mortalities were reported. A significant decrease in body weight gain and food consumption was seen in both sexes at the highest doses, but was attributed to unpalatability. At 475 mg/kg/day dams showed a significant increase in urine production with a lower specific gravity. Relative kidney weights were increased but were not dose-related in male rats. A significant increase in relative kidney and liver weight were seen in the dams at the highest dose; no histopathological changes were observed.
NOAEL (systemic toxicity$_{(M/F)}$) = 415/475 mg/kg/day (highest dose tested)

Reproductive Toxicity

Subcategory I: Benzaldehyde Derivatives
Benzaldehyde (CASRN 100-52-7)
See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
NOAEL (reproductive toxicity)$_{rat}$ = 800 mg/kg/day (highest dose tested)
NOAEL (reproductive toxicity)$_{mouse}$ = 1200 mg/kg/day (highest dose tested)

p-Methoxybenzaldehyde (CASRN 123-11-5)
In the combined repeated-dose/reproductive/developmental toxicity screening test described previously, reduced fertility index, number of pups/litter, delivery index and number of live pups was significantly reduced at 500 mg/kg/day. See human health data at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
LOAEL (reproductive toxicity) = 500 mg/kg/day (based on reduced fertility index, number of pups/litter, delivery index and number of live pups)
NOAEL (reproductive toxicity) = 100 mg/kg/day

Subcategory II: Benzyl and Benzoate Esters
Benzyl acetate (CASRN 140-11-4)
No typical reproductive toxicity studies are available on CASRN 140-11-4. However, the 13-week dietary studies in F344 rats and B6C3F1 mice described previously, sperm morphology and vaginal cytology examinations were conducted. Changes observed in absolute weights of the right cauda, epididymis and testes for male mice were not considered biologically significant. No changes were noted for sperm motility, density or morphology up to and including the highest dose tested (50,000 ppm; ~ 9400 mg/kg/day). High-dose (50,000 ppm; ~ 9400 mg/kg/day) dams exhibited an increase in mean estrus-cycle length, but the controls exhibited variations in cycle length as well. Male and female rats exhibited no effects on reproductive

organ weights, sperm motility, density or morphology up to and including the highest doses tested for these endpoints (25,000 ppm; ~ 1750 mg/kg/day in males and 1870 mg/kg/day in females).

Subcategory III: 2-Hydroxybenzoate Esters
Methyl 2-hydroxybenzoate (CASRN 119-36-8)
(1) In a three-generation reproductive toxicity study, Osborne-Mendel rats (20/sex/dose) were administered methyl 2-hydroxybenzoate in the diet at 0, 500, 1500, 3000 or 5000 ppm (~ 0, 25, 75, 150 or 250 mg/kg/day) from 100 days pre-mating through gestation. F_0 animals were mated twice to produce two F_1 litters (F_{1a} and F_{1b}). Selected F_1 offspring continued treatment and were mated to produce a third generation. There was no effect on parental survival or fertility index at any dose level. Effects on F_1 offspring at 150 and 250 mg/kg/day included statistically significant decreases in average litter size as well as decreases in the average number of live births per female and decreased survival. The statistically significant changes noted for the F_1 generation were not noted in the F_2 generation, although a decreasing trend was observed. There were no external abnormalities and necropsy revealed no changes.
NOAEL (parental toxicity) ~ 250 mg/kg/day (highest dose tested)
LOAEL (reproductive toxicity) ~ 150 mg/kg/day (based on decreased survival, average litter size and average number of live births per female)
NOAEL (reproductive toxicity) ~ 75 mg/kg/day
LOAEL (developmental toxicity) ~ 150 mg/kg/day (based on decreased survival)
NOAEL (developmental toxicity) ~ 75 mg/kg/day

(2) In a three-generation reproductive toxicity study, Wistar rats (25/sex/dose) were administered methyl 2-hydroxybenzoate in the diet at 0, 0.25 or 0.5 % (~ 0, 150 or 300 mg/kg/day for males and ~ 0, 125 or 250 mg/kg/day for females) for 60 days prior to mating and throughout the study. F_0 animals were mated twice to produce two F_1 litters (F_{1a} and F_{1b}). Selected F_1 animals were mated to produce the F_2 generation. No treatment-related effects were seen regarding mating and reproductive performance, number of stillborn, viability, mean litter size, number born, number live born or number of offspring alive at 5 days. No gross abnormalities were noted in the F_1 and F_2 generations. The robust summary did not include information regarding possible systemic parental toxicity.
NOAEL (reproductive toxicity) = 250 mg/kg/day (highest dose tested)

(3) Mice (25/sex/dose; strain unspecified) were administered methyl 2-hydroxybenzoate in the diet at 0, 0.25 or 0.5% (~ 0, 300 or 600 mg/kg/day) for 30 days prior to mating and throughout the study. F_0 animals were mated twice to produce two F_1 litters (F_{1a} and F_{1b}). Selected F_1 animals were mated to produce the F_2 generation. No effects on reproductive parameters including: mating and reproductive performance, number of stillborn, viability, mean litter size, number born, number live born or number of offspring alive at 5 days were noted. No gross abnormalities were noted in the F_1 and F_2 generations.
NOAEL (reproductive toxicity) ~ 600 mg/kg/day (highest dose tested)

(4) In a Fertility Assessment by Continuous Breeding (FACB) study conducted by NTP, CD-1 mice (20/sex/dose) were administered methyl 2-hydroxybenzoate via oral gavage at 100, 250 or 500 mg/kg/day throughout a 7-day pre-mating period, followed by a 100-day cohabitation period Treatment did not affect survival, clinical signs, body weights or fertility indices of parental mice. Significant decreases ($p < 0.05$) were noted for mean number of litters, average number of pups/litter, proportion of live births and mean live pup weights at 500 mg/kg/day.
NOAEL (parental toxicity) = 500 mg/kg/day (highest dose tested)
LOAEL (reproductive/developmental toxicity) = 500 mg/kg/day (based on decreased mean numbers of litters, number of pups/litter, proportion of live births and mean live pup weights)
NOAEL (reproductive toxicity) = 250 mg/kg/day

(5) CD-1 mice (20/sex/dose; 40/sex for controls) were exposed to methyl 2-hydroxybenzoate via gavage at 0, 25, 50 or 100 mg/kg/day throughout a 7-day pre-mating period, followed by a 98-day cohabitation period and a 21-day segregation period. No mortalities or clinical signs of toxicity were noted at any dose level for the F_0 or F_1 mice. Body weights were not affected by treatment and the fertility indexes were similar between treated F_0 mice and controls. There were no biologically significant treatment-related effects on the number of F_0 or F_1 pairs able to produce a litter, the number of live pups/litter or the male/female ratio.
NOAEL (systemic toxicity) = 100 mg/kg-bw/day (highest dose tested)
NOAEL (reproductive/developmental toxicity) = 100 mg/kg-bw/day (highest dose tested)

Developmental Toxicity

Subcategory I: Benzaldehyde Derivatives
p-Methoxybenzaldehyde (CASRN 123-11-5)
In the combined repeated-dose/reproductive/developmental toxicity screening test described previously, reduced fertility index, number of pups/litter, delivery index and number of live pups was significantly reduced at 500 mg/kg/day. See human health data at
http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
LOAEL (maternal toxicity) = 100 mg/kg/day (based on decreased body weight, decreased platelets and hypertrophy of hepatocytes)
NOAEL (maternal toxicity) = 20 mg/kg/day
LOAEL (developmental toxicity) = 500 mg/kg/day (based on reduced number of pups/litter, delivery index and number of live pups)
NOAEL (developmental toxicity) = 100 mg/kg/day

Subcategory II: Benzyl and Benzoate Esters
Benzyl acetate (CASRN 140-11-4)
Pregnant Wistar rats (20/dose) were administered benzyl acetate via oral gavage at 10, 100, 500 or 1000 mg/kg/day on gestation days (GDs) 6 – 15. An untreated control group was included. Dams were sacrificed on GD 20 and fetuses were examined for intrauterine death and internal, external and skeletal changes. There were no indications of maternal toxicity in any dose group. Fetal body weight was significantly decreased ($p < 0.05$) at 1000 mg/kg/day. Fetuses at 500 and 1000 mg/kg/day exhibited increased combined incidence of organ variations (slight dilatation of

the lateral ventricle and renal pelvis and presence of levo-umbilical artery) and the high-dose group exhibited increased skeletal variations including wavy ribs, dumb-bell shaped vertebrae, absence/splitting of thoracic vertebrae, presence of lumbar ribs and degree of ossification.
NOAEL (maternal toxicity) = 1000 mg/kg/day (highest dose tested**)**
LOAEL (developmental toxicity) = 500 mg/kg/day (based on increased combined incidence of organ and skeletal variations)
NOAEL (developmental toxicity) = 100 mg/kg/day

Subcategory III: 2-Hydroxybenzoate Esters
Methyl 2-hydroxybenzoate (CASRN 119-36-8)
(1) In a three-generation reproductive toxicity study previously described, Osborne-Mendel Rats (20/sex/dose) were administered methyl 2-hydroxybenzoate in the diet at 0, 500, 1500, 3000 or 5000 ppm (approximately 0, 25, 75, 150 or 250 mg/kg/day) from 100 days pre-mating through gestation. There was no effect on parental survival or fertility index at any dose level. Effects on F_1 offspring at 150 and 250 mg/kg/day included statistically significant decreases in average litter size as well as decreases in the average number of live births per female and decreased survival. The statistically significant changes noted for the F_1 generation were not noted in the F_2 generation, although a decreasing trend was observed. There were no external abnormalities and necropsy revealed no changes.
NOAEL (parental toxicity) ~ 250 mg/kg/day (highest dose tested)
LOAEL (developmental toxicity) ~ 150 mg/kg/day (based on decreased survival)
NOAEL (developmental toxicity) ~ 75 mg/kg/day

(2) In a three-generation reproductive toxicity study previously described, Wistar Rats (25/sex/dose) were administered methyl 2-hydroxybenzoate in the diet at 0, 0.25 or 0.5 % (approximately 0, 150 or 300 mg/kg/day for males and approximately 0, 125 or 250 mg/kg/day for females) for 60 days prior to mating and throughout the study. No treatment-related effects were seen regarding the number of stillborns, viability, mean litter size, number born, number live born or number of offspring alive at 5 days. No gross abnormalities were noted in the F_1 and F_2 generations. The robust summary did not include information regarding possible systemic parental toxicity.
NOAEL (reproductive toxicity) = 250 mg/kg/day (highest dose tested)

(3) In a NTP continuous breeding study, CD-1 mice (40/sex/dose) were administered 0, 50, 100, 250, 500 or 1000 mg/kg/day by oral gavage for ~100 days. Both sexes were treated 7 days premating. There were no treatment-related effects or any clinical signs of toxicity. Body weights were not affected by treatment and the fertility index was similar in all groups. At 1000 mg/kg/day, there was a significant decrease ($p<0.05$) in the mean number of litters, the average number of pups/litter, the proportion of pups born alive, and the mean live pup weights.
LOAEL (reproductive/developmental toxicity) = 1000 mg/kg/day (mortality and decrease in the number of litters, pups/litter and pup weights)
NOAEL (reproductive/developmental toxicity) = 500 mg/kg/day

Genetic Toxicity – Gene Mutation

In vitro

Subcategory I: Benzaldehyde Derivatives
Benzaldehyde (CASRN 100-52-7)
(1) Several studies are summarized in the SIDS documents. See human health data at
http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
Benzaldehyde was not mutagenic in these assays (see conclusion)**.**

(2) Several studies are summarized in the SIDS documents. See human health data at
http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
Benzaldehyde was mutagenic in these assays (see conclusion).

p-Methoxybenzaldehyde (CASRN 123-11-5)
(1) Several studies are summarized in the SIDS documents. See human health data at
http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
***p*-Methoxybenzaldehyde was mutagenic in these assays** (see conclusion).

(2) Several studies are summarized in the SIDS documents. See human health data at
http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
***p*-Methoxybenzaldehyde was not mutagenic in these assays** (see conclusion).

m-Methoxy-p-hydroxybenzaldehyde (CASRN 121-33-5)
Several studies are summarized in the SIDS documents. See human health data at
http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
***m*-Methoxy-*p*-hydroxybenzaldehyde was not mutagenic in these assays.**

Subcategory II: Benzyl and Benzoate Esters
Benzyl acetate (CASRN 140-11-4)
(1) In four separate Ames Assays, *Salmonella typhimurium* strains TA98, TA100, TA153, and/or 1535 were exposed to benzyl acetate at concentrations up to 10,000μg/plate in the presence and absence of metabolic activation in bacterial reverse mutation assays. Negative and positive controls were included, but the results were not provided. There was no increase in these revertants in any of these assays.
Benzyl acetate was not mutagenic in bacterial reverse mutation assays.

(2) Human TK6 lymphoblasts were exposed to benzyl acetate at concentrations up to 1500 μg/mL for 3 hours in the presence of metabolic activation or 20 hours in the absence of metabolic activation. Solvent and positive controls were tested concurrently; however, these responses were not included in the Robust Summary. Cytotoxicity was noted at 500μg/mL.
Benzyl acetate was mutagenic in the presence of S9 activation.

(3) Mouse lymphoma cells (L5178Y) were exposed to benzyl acetate at concentrations up to 1500 μg/mL for 4 hours in the presence and absence of metabolic activation. Solvent and positive controls were tested concurrently. Cytotoxicity was noted at 500 μg/mL.

Benzyl acetate was mutagenic in the presence of S9 activation.

(4) *Escherichia coli* WP2 uvrA (trp-) were exposed to benzyl acetate at concentrations up to 2000 µg/plate. Methodology, including use of metabolic activation and positive and negative controls, was not provided.
Benzyl acetate was not mutagenic in this assay.

(5) *Bacillus subtilis* M45 (Rec-) and H17 (Rec+) were exposed to benzyl acetate at concentrations up to 21 µL/disk in the absence of metabolic activation. Additional information, including the use of controls, was not provided. Benzyl acetate was reported to have an inhibition zone of < 2 mm, so was considered negative.
Benzyl acetate was not mutagenic in this assay.

Benzyl benzoate (CASRN 120-51-4)
Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 were exposed to benzyl benzoate at 0.03, 0.3, 3.0 or 30 µmol/plate. Cytotoxicity was not specified. Appropriate positive and negative control assays were conducted.
Benzyl benzoate was not mutagenic in this assay.

Methyl benzoate (CASRN 93-58-3)
Salmonella typhimurium strains TA97, TA98, TA100, TA1535 and TA1537 were exposed to methyl benzoate at concentrations ranging from 10 to 6666 µg/plate in the presence and without metabolic activation. Appropriate positive and negative controls were used.
Methyl benzoate was not mutagenic in this assay.

Methyl p-methylbenzoate (CASRN 99-75-2)
Salmonella typhimurium strains TA97, TA98, TA100, TA1535 and TA1537 were exposed to methyl *p*-methylbenzoate at concentrations ranging from 10 to 6666 µg/plate in the presence and absence of metabolic activation. Appropriate positive and negative controls were tested concurrently.
Methyl *p*-methylbenzoate was not mutagenic in this assay.

Subcategory III: 2-Hydroxybenzoate Esters
Methyl 2-hydroxybenzoate (CASRN 119-36-8)
(1) *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 were exposed to methyl 2-hydroxybenzoate at 0, 1, 3.3, 10, 33.3, 100 or 333µg/plate in the presence and absence of metabolic. Appropriate positive and negative controls were tested concurrently and there was no indication that the response was not as expected.
Methyl 2-hydroxybenzoate was not mutagenic in this assay.

(2) *Salmonella typhimurium* strains TA92, TA94, TA98, TA100, AND TA1535 were exposed to methyl 2-hydroxybenzoate (99% purity) at concentrations up to 10 mg/plate in the presence and absence of metabolic activation in several bacterial reverse mutation assays. Information concerning the use of positive and negative controls was not provided and additional study details were not given.
Methyl 2-hydroxybenzoate was not mutagenic in this assay.

(3) *Salmonella typhimurium* strains TA98 and TA100 were exposed to methyl 2-hydroxybenzoate at 0.1 mg/plate in the presence and absence of metabolic activation from PCB-treated livers of male SD rats, ddY mice, golden hamsters or Hartley guinea pigs. Positive controls were used, but the results were not provided. The number of revertants/plate was increased only with the addition of S9 mix from hamster liver in the presence of metabolic activation.
Methyl 2-hydroxybenzoate was mutagenic in the presence of S9 activation from hamster liver.

(4) *Bacillus subtilis* (M45 Rec- and H17 Rec+) plate cultures were exposed to methyl 2-hydroxybenzoate via saturated discs at up to 5 mg/disc in several reverse mutagenicity assays. Mutagenic potential was calculated by measuring the zone of growth inhibition surrounding the discs.
Methyl 2-hydroxybenzoate was not mutagenic in these assays.

Benzyl 2-hydroxybenzoate (CASRN 118-58-1)
Salmonella typhimurium strains TA98, TA100, TA1535, and TA1537 were exposed to benzyl 2-hydroxybenzoate at concentrations ranging from 0.3, 1.0, 3.3, 10, 20, 33, 100, 333, and 666 µg/plate in the presence and absence of metabolic activation. Appropriate positive and negative controls were included with no indication that the results were not as expected.
Benzyl 2-hydroxybenzoate was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro

Subcategory I: Benzaldehyde Derivatives
Benzaldehyde (CASRN 100-52-7)
(1) Several studies are summarized in the SIDS documents. See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
Benzaldehyde induced chromosome aberrations in these assays, depending on the cell line (see conclusion)**.**

(2) Several studies are summarized in the SIDS documents. See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
Benzaldehyde induced sister chromatid exchange in these assays, depending on the cell line (see conclusion)**.**

p-Methoxybenzaldehyde (CASRN 123-11-5)
(1) See human health data at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
***p*-Methoxybenzaldehyde did not induce sister chromatid exchange in cells without mitomycin-C pre-treatment.**

(2) See human health data at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
***p*-Methoxybenzaldehyde induced sister chromatid exchanges in this assay.**

(3) Several studies are summarized in the SIDS documents. See human health data at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=413df70f-f309-4eb4-8278-1da434eda903&idx=0
***p*-Methoxybenzaldehyde induced chromosomal aberrations in these assays, depending on the cell line** (see conclusion)**.**

m-Methoxy-p-hydroxybenzaldehyde (CASRN 121-33-5)
(1) Several studies are summarized in the SIDS documents. See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
***m*-Methoxy-*p*-hydroxybenzaldehyde did not induce chromosomal aberrations in these assays, depending on the cell line** (see conclusion)**.**

(2) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
***m*-Methoxy-*p*-hydroxybenzaldehyde induced sister chromatid exchanges in these assays, depending on the cell line** (see conclusion)**.**

Subcategory II: Benzyl and Benzoate Esters
Benzyl Acetate (CASRN 140-11-4)
(1) Chinese hamster lung fibroblasts were exposed to benzyl acetate at 0 – 2.4 mg/mL in the presence and absence of metabolic activation for 6 hours or 24 or 48 hours in the absence of metabolic activation. Negative (solvent) and positive controls were tested, but the responses were not provided. Precipitate was seen at ≥ 0.6 mg/mL, while cytotoxicity was noted at 0.9 mg/mL.
Benzyl acetate did not induce chromosomal aberrations in this assay.

(2) Chinese hamster ovary cells were exposed to benzyl acetate at 160 – 1600 µg/mL in the absence of metabolic activation or 500 – 5000 µg/mL in the presence of metabolic activation. Negative (solvent) and positive controls were tested, but the responses were not provided.
Benzyl acetate did not induce chromosomal aberrations in this assay.

(3) Chinese hamster ovary cells were exposed to benzyl acetate at 50 – 500 µg/mL n the absence of metabolic activation or 500 – 5000 µg/mL in the presence of metabolic activation in a sister chromatid exchange assay.
Benzyl acetate did not induce sister chromatid exchanges in this assay.

Subcategory III: 2-Hydroxybenzoate Esters
Methyl 2-hydroxybenzoate (CASRN 119-36-8)
(1) Human embryo fibroblast cells were exposed to methyl 2-hydroxybenzoate at unspecified concentrations with and without metabolic activation. No information concerning the use of positive and negative controls was provided and no additional details were given.
Methyl 2-hydroxybenzoate did not induce sister chromatid exchanges or aberrations in these assays.

(2) Chinese hamster fibroblasts were exposed to methyl 2-hydroxybenzoate at concentrations up to 0.25 mg/mL in the absence of metabolic activation for 24 or 48 hours. Negative and solvent-treated controls were tested. The incidence of polyploid cells and structural chromosomal aberrations were counted in 100 well-spread metaphases.
Methyl 2-hydroxybenzoate did not induce chromosomal aberrations in this assay.

In vivo

Subcategory I: Benzaldehyde Derivatives
m-Methoxy-p-hydroxybenzaldehyde (CASRN 121-33-5)
See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
***m*-Methoxy-*p*-hydroxybenzaldehyde did not induce mouse micronuclei in these assays.**

Subcategory II: Benzyl and Benzoate Esters
Benzyl Acetate (CASRN 140-11-4)
Male B6C3F1 mice (5 – 7/dose) were administered benzyl acetate via intraperitoneal injection at 0, 312, 625 or 1250 mg/kg/day for 3 days in a micronucleus assay. Positive controls were administered dimethyl benzyl(a) anthracene (DMBA). Twenty-four hours after the final treatment, the mice were sacrificed and bone marrow slides were prepared and evaluated for number of micronucleated-polychromatic erythrocytes (MPE). The mitotic index and the ratio of polychromatic erythrocytes (PCE) to normo-chromatic erythrocytes (NCE) were also determined.
Benzyl acetate did not induce the formation of micronuclei in this assay.

Genetic Toxicity – Other

In vitro

Subcategory I: Benzaldehyde Derivatives
Benzaldehyde (CASRN 100-52-7)
See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
Benzaldehyde did not induce unscheduled DNA synthesis in this assay.

m-Methoxy-p-hydroxybenzaldehyde (CASRN 121-33-5)
See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf
***m*-Methoxy-*p*-hydroxybenzaldehyde did not induce unscheduled DNA synthesis in this assay.**

Subcategory II: Benzyl and Benzoate Esters
Benzyl Acetate (CASRN 140-11-4)
Male F344 rat hepatocytes were exposed to benzyl acetate at unspecified concentrations in an unscheduled DNA synthesis (UDS) assay. Additional details were not provided. Positive controls were tested but the results not provided.
Benzyl acetate did not induce unscheduled DNA synthesis in this assay.

In vivo

Subcategory II: Benzyl and Benzoate Esters
Benzyl Acetate (CASRN 140-11-4)
(1) Male F344 rats (1/dose) were administered benzyl acetate via single intraperitoneal injection of 0, 150, 500 or 1500 mg/kg/day. One hour following administration, the rats were sacrificed and nuclei were isolated from the pancreas for evaluation of DNA damage.
Benzyl acetate did not induce DNA damage in this assay.

(2) Male F344 rats (number not specified) were administered benzyl acetate via gavage at 0, 50, 200 or 1000 mg/kg/day. Two or 24 hours following treatment, the rats were sacrificed and hepatocytes cultures were prepared for analysis of unscheduled DNA synthesis (UDS).
Benzyl acetate did not induce unscheduled DNA synthesis in this assay.

Additional Information

Skin Irritation

Subcategory I: Benzaldehyde Derivatives
***m*-Methoxy-*p*-hydroxybenzaldehyde (CASRN 121-33-5)**
Two skin irritation studies in rabbits [Food and Cosmetics Toxicology, 1963-81] and guinea pigs [NTIS OTS0533624, 1991] were reported, although the data have low reliability because no details of the studies were available. The skin irritation was reported to be moderate in the study using rabbits (500 mg/kg/24h) and slight to moderate in the study using guinea pigs (1.0-10 ml/kg/24h). The SIAP states that
CASRN 123-11-5 is irritating to rabbit and guinea pig skin.
See human health data at http://webnet.oecd.org/hpv/UI/handler.axd?id=eeeb5caa-7de8-4e20-b423-a0421d029f66

Carcinogenicity

Subcategory I: Benzaldehyde Derivatives
Benzaldehyde (CASRN 100-52-7)
(1) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
In a two-year study, B6C3F1 mice (50/sex/dose) were exposed to CASRN 100-52-7 by oral gavage at 200 or 400 mg/kg/day (males) and 300 or 600 mg/kg/day (females). No treatment-related effects on mortality, clinical signs and body weight were observed.
The incidence of focal hyperplasia and squamous cell papillomas of the forestomach were significantly increased in mice of both sexes.

(2) See human health data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/100527.pdf
In a two-year study, F334/N rats (50/sex/dose) were exposed to CASRN 100-52-7 by oral gavage at 200 or 400 mg/kg/day. Mortality was significantly increased in high dose males. No treatment-related effects on clinical signs and body weight were observed.
There was no increased incidence of tumors in rats.

Subcategory II: Benzyl and Benzoate Esters
Benzyl acetate (CASRN 140-11-4)
(1) Male F344 rats (25/dose) were administered benzyl acetate in the diet at 0.8% (~ 400 mg/kg/day) for 2 years. Necropsy revealed anaplastic changes and desmoplasia in all groups, including the control (basal diet). An 8% increase in the incidence of pancreatic carcinoma was noted for rats receiving benzyl acetate compared to controls (0%).
Benzyl acetate is a weak promoter of pancreatic carcinogenesis in rats.

(2) In an NTP study, B6C3F1 mice (60/sex/dose) were administered benzyl acetate in the diet for 103 weeks at concentrations of 0, 330, 1000 or 3000 ppm (~ 0, 35, 110 or 345 mg/kg/day and 0, 40, 130 or 375 mg/kg/day for male and female mice, respectively). Survival of was not adversely affected by treatment. The mean body weights of males and females at 3000 and 1000 ppm were 2 – 14% lower than controls. No increase in neoplasm incidence in mice could be attributed to benzyl acetate administration in feed. This is in contrast with the previous finding that administration of benzyl acetate in corn oil by gavage once daily 5 days a week for as long as 2 years was carcinogenic to mice, causing increased incidences of hepatocellular neoplasms and forestomach neoplasms. The contrast in results between the two studies may be due to differences in the dose levels used (highest dose: gavage, 1,000 mg/kg a day; feed, 360 mg/kg a day). Dose-related increased incidences or severities of nonneoplastic nasal lesions occurred in the most posterior portions of the nasal cavity in all exposed groups. The lesions occurred in the majority of the exposed mice and consisted of atrophy and degeneration, primarily of the olfactory epithelium, cystic hyperplasia of the nasal submucosal glands, pigmentation of the mucosal epithelium, and exudate accumulation. Hematological and clinical chemistry analysis revealed no treatment-related effects.
Benzyl acetate did not show evidence of neoplasms or nonneoplastic lesions in mice under the conditions of this assay.

(3) In an NTP study, F344 rats (60/sex/dose) were administered benzyl acetate in the diet for 103 weeks at concentrations of 0, 3000, 6000 or 12,000 ppm (~ 0, 130, 260 or 510 mg/kg/day for males and ~ 0, 145, 290 or 575 mg/kg/day for females). The mean body weights of both sexes at12,000 ppm were approximately 5% lower than those of the controls throughout most of the study. Food consumption was also decreased at this dose level in both sexes. No effects were seen regarding survival, hematology or clinical chemistry. No changes in the incidence of neoplastic and non-neoplastic lesions were noted.
Benzyl acetate did not show evidence of neoplasms or nonneoplastic lesions in rats under the conditions of this assay.

(4) In an NTP study, B6C3F1 mice (50/sex/dose) were administered benzyl acetate via oral gavage at 0, 500 or 1000 mg/kg/day, 5 days/week for 103 weeks. Survival was not adversely affected by treatment. An infection in the genital tract was probably responsible for the deaths in controls (26/35), at 500 (14/32), and at 1000 (8/20) mg/kg/day in females before the end of the study. No clinical signs of toxicity were noted and the body weights of treated females were slightly higher than controls. A statistically significant increase in the incidence of hepatocellular adenomas was seen in males and females at 3000 mg/kg/day ($p < 0.001$and $p < 0.05$, respectively), and a significant increase in forestomach hyperplasia was noted in both sexes

($p < 0.005$). Squamous cell papillomas or carcinomas of the forestomach (uncommon neoplasms) occurred with a positive trend ($P<0.05$) in male mice (4/49; 4/48; 11/49). The incidence of these tumors was also marginally ($P=0.054$) increased in the high-dose female mice (0/50; 0/50; 4/48). The incidences of these tumors in both the high-dose male and the high-dose female mice were considerably higher than the historical corn oil gavage control rates at this laboratory (males, 2/296, 0.7%; females, 2/297, 0.7%) and throughout the study (males, 14/1,070, 1.3%; females, 3/1,073, 0.3%). Forestomach hyperplasia occurred at increased incidences in dosed mice of either sex (males: 1/49, 7/48, 22/49; females: 1/50, 6/50, 17/48). The neoplasms and hyperplasia of the forestomach were probably related to administration of benzyl acetate.
Benzyl acetate increased the incidence of hepatocellular adenomas and squamous cell neoplasms of the forestomach in mice under the conditions of this study.

(5) In an NTP study, F344 rats (50/sex/dose) were administered benzyl acetate via gavage at 0, 250 or 500 mg/kg/day, 5 days/week for 103 weeks. No mortalities were noted. Pancreatic acinar-cell hyperplasia was noted for all male groups, while the incidence of multiple acinar-cell adenomas was significantly increased ($p < 0.01$) in high-dose males when compared to controls, but not in females at any dose level. Preputial gland neoplasms occurred with a positive trend ($P<0.05$) in male rats (cystadenocarcinoma: 0/50; 0/50; 3/50; all adenocarcinoma: 0/50; 1/50; 4/50; adenocarcinoma or carcinoma combined: 1/50; 1/50; 6/50). However, the incidence of all preputial gland tumors was not significantly elevated (2/50; 1/50; 6/50). For female rats the incidence of clitoral gland neoplasms was marginally increased (2/50; 0/50; 5/50).
Benzyl acetate increased the incidence of pancreatic acinar-cell adenomas in male rats under the conditions of this study.

Conclusions:

Subcategory I: Benzaldehyde Derivatives

The acute oral toxicity of subcategory I members is low in rats and guinea pigs. The acute dermal toxicity of CASRN 100-52-7 is moderate in rabbits. In several National Toxicology Program (NTP) and other 13-week oral repeated-dose toxicity studies, CASRN 100-52-7 showed histopathological changes in various organ systems at 800 mg/kg/day in rats, and renal lesions and decreased body weight changes in male mice at 600 mg/kg/day. The NOAELs for systemic toxicity were 400 mg/kg/day and 300 mg/kg/day in rats and mice, respectively. No specific reproductive toxicity studies are available for CASRN 100-52-7; however, in the 13-week oral repeated-dose toxicity studies in rats and mice, no treatment related effects on reproductive organs were observed. CASRN 100-52-7 was not mutagenic in bacteria and mammalian cells *in vitro.* CASRN 100-52-7 induced chromosome aberrations in mammalian cells *in vitro* and was positive for sister chromatid exchanges in human lymphocytes *in vitro.* CASRN 100-52-7 did not induce unscheduled DNA synthesis in rat hepatocytes *in vitro.* CASRN 100-52-7 did not show an increased incidence of tumors in rats but showed an increase in the incidence of focal hyperplasia and squamous cell papillomas of the forestomach in mice.

The acute dermal toxicity of CASRN 123-11-5 is low in rabbits. The acute inhalation (vapor) toxicity of CASRN 123-11-5 in rats is high. In two oral repeated-dose toxicity studies with

CASRN 123-11-5 in rats, no systemic effects were seen in rats; the NOAELs for systemic toxicity were 50 mg/kg/day (13 weeks; only dose tested) and 500 mg/kg/day (29-weeks; only dose tested). In a combined oral repeated-dose/reproductive/developmental toxicity screening test with CASRN 123-11-5, decreased body weights, decreased platelets and hypertrophy of hepatocytes were noted at 100 mg/kg/day; the NOAEL for systemic toxicity was 20 mg/kg/day. CASRN 123-1-5 showed significantly reduced fertility index, number of pups/litter, delivery index and number of live pups at 500 mg/kg/day; the NOAEL for reproductive/developmental toxicity was 100 mg/kg/day. CASRN 123-11-5 was not mutagenic in bacteria but mutagenic in mouse lymphoma cells *in vitro*. CASRN 123-11-5 induced chromosomal aberrations in Chinese Hamster Ovary (CHO) cells but not in fibroblast cells *in vitro*. CASRN 123-11-5 was positive for sister chromatid exchange in human lymph oocytes but not CHO cells *in vitro*.

In 16 to 28-week oral repeated-dose toxicity studies, CASRN 121-33-5 showed no treatment-related effects in rats and dogs; the NOAELs for systemic toxicity ranged from 50 (highest dose tested) to 500 mg/kg/day (only dose tested) in rats; the NOAEL for systemic toxicity for dogs was 100 mg/kg/day (highest dose tested). CASRN 121-33-5 was not mutagenic in bacteria and mouse lymphoma cells *in vitro*. CASRN 121-33-5 induced chromosomal aberrations in human lymphocytes but did not induce chromosomal aberrations in CHO cells and Chinese hamster fibroblasts *in vitro*. CASRN 121-33-5 induced sister chromatid exchanges in human lymphocytes but not in CHO cells *in vitro*. CASRN 121-33-5 did not induce unscheduled DNA synthesis in rat hepatocytes *in vitro*. CASRN 121-33-5 did not induce mouse micronuclei *in vivo*. CASRN 121-33-5 is irritating to rabbit and guinea pig skin.

Subcategory II: Benzyl and Benzoate Esters

The acute oral toxicity of subcategory II members is low in rats, mice, rabbits, guinea pigs, and dogs. The acute inhalation toxicity of CASRN 93-58-3 is moderate in rats. The acute dermal toxicity of CASRN 120-51-4 in rats is low; and the acute dermal toxicity of CASRNs 93-58-3 and 99-75-2 in rabbits is low. In a 28-day repeated-dose toxicity study with CASRN 140-11-4, a significant decrease in body weight, absolute brain weight and mortality were seen in rats at 2000 mg/kg/day; the NOAEL for systemic toxicity was not established. Several NTP 13-week repeated-dose toxicity studies are available for rats and mice. Mice studies showed decreased final mean body weight and body weight gain, and relative and absolute organ weights in various organs of both sexes at 650 mg/kg/day (females) and 425 mg/kg/day (males); the NOAELs were not established for mice. Male rats showed testicular atrophy, decreased body weight gain, and mortality at dose ranges of 900 to 1000 mg/kg/day; the lowest rat NOAEL for systemic toxicity was 460 mg/kg/day. No specific reproductive toxicity studies are available; however, in the13-week dietary studies in rats and mice, no significant treatment related effects were observed on sperm morphology and vaginal cytology examinations. In an oral prenatal developmental toxicity study in rats, no maternal toxicity was seen. An increase in combined organ and skeletal variations were seen in the fetus at 500 mg/kg/day. The NOAEL for maternal and developmental toxicity was 1000 mg/kg/day (highest dose tested) and 100 mg/kg/day, respectively. CASRNs 120-51-4, 93-58-3 and 99-75-2 were not mutagenic in bacteria *in vitro*. CASRN 140-11-4 was mutagenic in human lymphoblasts and mouse lymphoma cells but not mutagenic in bacteria *in vitro*. CASRN 140-11-4 did not induce chromosomal aberrations or sister chromatid exchange in CHO cells *in vitro*. CASRN 140-11-4 did not induce mouse micronuclei *in vivo* or unscheduled DNA synthesis in rats *in vitro or in vivo*. Several two-year chronic/carcinogenicity studies were conducted with rats and mice by NTP. CASRN 140-11-4 showed evidence of pancreatic tumors in male rats. In the two-year study with rats and mice via oral gavage, CASRN 140-11-4 showed increased incidence of pancreatic acinar-cell adenomas in rats; hepatocellular adenomas and squamous cell neoplasms of the forestomach in mice. In two-year dietary studies in rats and mice, CASRN 140-11-4 showed no evidence of neoplasms in rats or mice.

Subcategory III: 2-Hydroxybenzoate Esters
The acute oral toxicity of CASRN 119-36-8 is low in rats and mice. The acute oral toxicity of CASRN 118-58-1 is low in rats. The acute oral and dermal toxicity of CASRN 2050-08-0 is low in rats and rabbits, respectively. In an oral repeated-dose toxicity study with CASRN 2050-08-0 in rats, the LOAEL and NOAEL could not be established due to equivocal results for systemic toxicity in both sexes. In a 30-week dietary repeated-dose toxicity study in rats, decreased body weight gain was seen in both sexes at 315 (males) and 565 mg/kg/day (females); the NOAEL for systemic toxicity was 180 mg/kg/day and 315 mg/kg/day for males and females, respectively. A six-month oral repeated-dose toxicity study with CASRN 119-36-8 in dogs showed no adverse toxic effects; the NOAEL for systemic toxicity in dogs was 167 mg/kg/day (highest dose tested). However, dogs treated for two years by the same route, showed decreased growth and enlarged livers at 150 mg/kg/day; the NOAEL for systemic toxicity was 50 mg/kg/day. In two, three-generation dietary reproductive toxicity studies in rats with CASRN 119-36-8, no parental toxicity was observed up to 250 mg/kg/day (highest dose tested). In the first study, decrease in litter survival, and a decrease in average litter size and average number of live births per female was noted at 150 mg/kg/day; the NOAEL for reproductive/developmental toxicity was 75 mg/kg/day. In the second study, a decrease in mean number of litters, number of pups/litter, proportion of live births and mean live pup weights was observed at and above 500 mg/kg/day; the NOAEL for reproductive/developmental toxicity was 250 mg/kg/day. In a continuous breeding study in mice, CASRN 119-36-8 showed no treatment-related effects in adults up to 1000 mg/kg/day (highest dose tested) and decreased mean numbers of litters, number of pups/litter, proportion of live births and mean live pup weights at 1000 mg/kg/day; the NOAEL for reproductive/developmental toxicity was 500 mg/kg/day. CASRNs 119-36-8 and 118-58-1 were not mutagenic in bacteria *in vitro*. CASRN 119-36-8 did not induce chromosomal aberrations or sister chromatid exchange *in vitro*.

Table 5. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data

Endpoints	***Subcategory I***			***Subcategory II***				***Subcategory III***		
	Benzaldehyde Derivatives			***Benzyl and Benzoate Esters***				***2-Hydroxybenzoate Esters***		
	Benzaldehyde **(100-52-7)**	***p*-Methoxy-benzaldehyde** **(123-11-5)**	***m*-Methoxy-*p*-hydroxy-benzaldehyde** **(121-33-5)**	**Benzyl acetate** **(140-11-4)**	**Benzyl benzoate** **(120-51-4)**	**Methyl benzoate** **(93-58-3)**	**Methyl *p*-methyl benzoate** **(99-75-2)**	**Methyl 2-hydroxy benzoate** **(119-36-8)**	**Pentyl 2-hydroxy benzoate** **(2050-08-0)**	**Benzyl 2-hydroxy benzoate** **(118-58-1)**
Acute Oral Toxicity LD$_{50}$ (mg/kg-bw)	**1000**	**1260**	**1400**	**2490**	**~ 1100**	**2170**	**3300**	**887**	**4100**	**2227**
Acute Inhalation Toxicity LC$_{50}$ (mg/L)	No Data > 0.32 (RA)	**> 0.32** **(vapor)**	No Data > 0.32 (RA)	No Data > 5.57 (RA)	No Data > 5.57 (RA)	**> 5.57**	No Data > 5.57 (RA)	–	–	–
Acute Dermal Toxicity LD$_{50}$ (mg/kg-bw)	**> 1250**	**> 5000**	No Data > 1250 (RA)	No Data > 2000 (RA)	**~ 4000**	**> 2000**	**> 5000**	No Data > 5000 (RA)	**> 5000**	No Data > 5000 (RA)
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg/day)	**(rat; 13-week)** **NOAEL = 400** **LOAEL = 800** **(mouse; 13-week)** **NOAEL = 600** **LOAEL = 300**	**(rat)** **NOAEL = 20** **LOAEL = 100**	**(rat; 26 week)** **NOAEL = 437** **(highest dose tested)** **(dog; 26 week)** **NOAEL = 100** **(highest dose tested)**	**(rat)** **NOAEL$_f$ ~ 930** **LOAEL$_f$ ~ 480** **NOAEL$_m$ ~ 900** **LOAEL$_m$ ~ 460** **(mouse)** **NOAEL$_{f/m}$ ~ not established** **LOAEL$_m$ ~ 425** **LOAEL$_f$ ~ 650**	No Data (rat) NOAEL$_f$ ~ 930 LOAEL$_f$ ~ 480 NOAEL$_m$ ~ 900 LOAEL$_m$ ~ 460 (mouse) NOAEL$_{f/m}$ ~ not established LOAEL$_m$ ~ 425 LOAEL$_f$ ~ 650 (RA)	No Data (rat) NOAEL$_f$ ~ 930 LOAEL$_f$ ~ 480 NOAEL$_m$ ~ 900 LOAEL$_m$ ~ 460 (mouse) NOAEL$_{f/m}$ ~ not established LOAEL$_m$ ~ 425 LOAEL$_f$ ~ 650 (RA)	No Data (rat) NOAEL$_f$ ~ 930 LOAEL$_f$ ~ 480 NOAEL$_m$ ~ 900 LOAEL$_m$ ~ 460 (mouse) NOAEL$_{f/m}$ ~ not established LOAEL$_m$ ~ 425 LOAEL$_f$ ~ 650 (RA)	**(rat; 30 week)** **NOAEL$_m$= 180** **LOAEL$_m$ = 315** **NOAEL$_f$ = 315** **LOAEL$_f$ = 565** **(dog; 26 week)** **NOAEL = 167** **(highest dose tested)** **(dog; 2 years)** **NOAEL = 50** **LOAEL = 150**	No Data (rat; 30 week) NOAEL$_m$= 180 LOAEL$_m$ = 315 NOAEL$_f$ = 315 LOAEL$_f$ = 565 (dog; 26 week) NOAEL = 167 (dog; 2 years) NOAEL = 50 LOAEL = 150 (RA)	No Data (rat; 30 week) NOAEL$_m$= 180 LOAEL$_m$ = 315 NOAEL$_f$ = 315 LOAEL$_f$ = 565 (dog; 26 week) NOAEL = 167 (dog; 2 years) NOAEL = 50 LOAEL = 150 (RA)
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg/day)	**(rat)** **NOAEL = 800** **(highest dose tested)**	**(rat)** **NOAEL = 100** **LOAEL = 500**	No Data NOAEL = 100 LOAEL = 500 (RA)	There are no specific reproductive toxicity studies available for the subcategory II members; however, no adverse effects were observed on the reproductive organs in the 13-week oral repeated-dose toxicity studies in rats and mice with CASRN 140-11-4.				**(rat)** **NOAEL = 150** **LOAEL = 75** **(mouse)** **NOAEL = 150** **LOAEL = 75**	No Data (rat) NOAEL = 150 LOAEL = 75 (mouse) NOAEL = 150 LOAEL = 75 (RA)	No Data (rat) NOAEL = 150 LOAEL = 75 (mouse) NOAEL = 150 LOAEL = 75 (RA)

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Endpoints	***Subcategory I***			***Subcategory II***				***Subcategory III***		
	Benzaldehyde Derivatives			***Benzyl and Benzoate Esters***				***2-Hydroxybenzoate Esters***		
	Benzaldehyde **(100-52-7)**	***p*-Methoxy-benzaldehyde** **(123-11-5)**	***m*-Methoxy-*p*-hydroxy-benzaldehyde** **(121-33-5)**	**Benzyl acetate** **(140-11-4)**	**Benzyl benzoate** **(120-51-4)**	**Methyl benzoate** **(93-58-3)**	**Methyl *p*-methyl benzoate** **(99-75-2)**	**Methyl 2-hydroxy benzoate** **(119-36-8)**	**Pentyl 2-hydroxy benzoate** **(2050-08-0)**	**Benzyl 2-hydroxy benzoate** **(118-58-1)**
Developmental Toxicity NOAEL/LOAL Oral (mg/kg/day) **Maternal Toxicity** **Developmental Toxicity** **Maternal Toxicity** **Developmental Toxicity**	No Data (rat) NOAEL = 20 LOAEL = 100 NOAEL = 100 LOAEL = 500 (RA)	**(rat)** **NOAEL = 100** **LOAEL = 20** **NOAEL = 100** **LOAEL = 500**	No Data (rat) NOAEL = 20 LOAEL = 100 NOAEL = 100 LOAEL = 500 (RA)	**NOAEL = 1000** **(highest dose tested)** **NOAEL = 100** **LOAEL = 500**	No Data NOAEL = 1000 NOAEL = 100 LOAEL = 500 (RA)	No Data NOAEL = 1000 NOAEL = 100 LOAEL = 500 (RA)	No Data NOAEL = 1000 NOAEL = 100 LOAEL = 500 (RA)	**(rat)** **NOAEL = 250** **(highest dose tested)** **NOAEL = 75** **LOAEL = 150** **(mouse)** **NOAEL = 500** **(highest dose tested)** **NOAEL = 250** **LOAEL = 500**	No Data (rat) NOAEL = 250 NOAEL = 75 LOAEL = 150 (mouse) NOAEL = 500 NOAEL = 250 LOAEL = 500 (RA)	No Data (rat) NOAEL = 250 NOAEL = 75 LOAEL = 150 (mouse) NOAEL = 500 NOAEL = 250 LOAEL = 500 (RA)
Genetic Toxicity – Gene Mutation *In vitro*	**Positive**	**Positive**	**Negative**	**Negative**	**Negative**	**Negative**	**Negative**	**Positive**	No Data Positive (RA)	**Negative**
Genetic Toxicity – Chromosomal Aberrations *In vitro*	**Positive**	**Positive**	**Negative**	**Negative**	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	**Positive**	No Data Positive (RA)	No Data Positive (RA)
Genetic Toxicity – Chromosomal Aberrations *In vivo*	–	–	**Negative**	**Negative**	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	–	–	–
Genetic Toxicity – Other Unscheduled DNA Synthesis *In vitro*	**Negative**	–	**Negative**	**Negative**	–	–	–	–	–	–

Table 5. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data

Endpoints	*Subcategory I*			*Subcategory II*				*Subcategory III*		
	Benzaldehyde Derivatives			*Benzyl and Benzoate Esters*				*2-Hydroxybenzoate Esters*		
	Benzaldehyde (100-52-7)	***p*-Methoxy-benzaldehyde (123-11-5)**	***m*-Methoxy-*p*-hydroxy-benzaldehyde (121-33-5)**	**Benzyl acetate (140-11-4)**	**Benzyl benzoate (120-51-4)**	**Methyl benzoate (93-58-3)**	**Methyl *p*-methyl benzoate (99-75-2)**	**Methyl 2-hydroxy benzoate (119-36-8)**	**Pentyl 2-hydroxy benzoate (2050-08-0)**	**Benzyl 2-hydroxy benzoate (118-58-1)**
Genetic Toxicity – Other Unscheduled DNA Synthesis *In vivo*	**Negative**	–	–	**Negative**	–	–	–	–	–	–
Additional Information Skin Irritation Rabbit Guinea Pig	–	**Positive Positive**	–	–	–	–	–	–	–	–
Additional Information Carcinogenicity	**(mouse) Positive (rat) Negative**	–	–	**Diet (mouse) Negative (rat) Negative Gavage (mouse) Positive (rat) Positive**	–	–	–	–	–	–

Measured data in bold; RA = read across; − indicates endpoint not addressed for this chemical; f = female; m=male

4. Hazard to the Environment

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 6. The table also indicates where data for tested subcategory members are read-across (RA) to untested members of each subcategory. Aquatic data from two previous SIDS cases included in Table 6 were obtained from: CASRN 121-33-5 (http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf) and CASRN 123-11-5 [SIAP is only available; SIAR/robust summaries are not yet publicly available] (http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=624478ca-b163-434a-8b6c-bae2cfa08e0c&idx=0).

Since these chemical category members are volatile and testing performed with nominal concentrations may underestimate toxicity, the estimated ecotoxicity values may be used in support of these chemicals' experimental results.

Acute Toxicity to Fish

Subcategory I: Aldehydes
Benzaldehyde (CASRN 100-52-7)
Fathead minnow *(Pimephales promelas)* were exposed to benzaldehyde (98% purity) at nominal concentrations of 8.6, 14.3, 23.9, 39.8, 66.3 mg/L for 96 hours. Dissolve oxygen content was 7.2 mg/L, water hardness 46.2 mg/L $CaC0_3$, pH 7.73, temperature 23.9 Celsius. LC_{50} value reported is analytically measured and supplied as new data to this submission (*Brook et al*., 1984)
96-h LC_{50} = 7.61 mg/L

p-Methoxybenzaldehyde (CASRN 123-11-5)
See fish toxicity data at http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=624478ca-b163-434a-8b6c-bae2cfa08e0c&idx=0).

Subcategory II: Esters
Benzyl Acetate (CASRN 140-11-4)
(1) Japanese medaka (*Oryzias latipes*) were exposed to benzyl acetate (99% purity) for at least 96 hours at measured concentrations of <0.25, 1.48, 2.45, 4.43, 8.81, and 19.8 mg/L in a flow-through test system. Twenty fish per concentration and ten per replicate were used in the acute test. Concentrations and test conditions were supplied as new data to this submission.
96-h LC_{50} = 4.0 mg/L

(2) Zebra fish (*Danio rerio*) were exposed to benzyl acetate at nominal concentrations of 5.5, 7.8, 11, 16 or 22 mg/L under static-renewal conditions for 96 hours. Test concentrations were measured at the end of each 24-hour period. The mortality rates at 16 and 22 mg/L were 60 and 100%, respectively. Sluggish swimming was exhibited by fish in the 16 mg/L group. No mortality or clinical signs were noted at concentrations ≤ 11 mg/L.
96-h LC_{50} = 7.9 mg/L

Benzyl benzoate (CASRN 120-51-4)
Zebra fish (*Danio rerio*) were exposed to benzyl benzoate at 3.9, 5.5, 7.8 or 11 mg/L under static-renewal conditions 96 hours. Test concentrations were measured (GC analysis) at the beginning and end of each day. The mortality rate was 100% at ≥ 5.5 mg/L. Fish at 5.5 mg/L exhibited sluggish swimming.
96-h LC_{50} = 1.34 mg/L

Methyl benzoate (CASRN 93-58-3)
Bluegill sunfish (*Lepomis macrochirus*) were exposed to methyl benzoate at concentrations of 0 (solvent control), 5, 10, 20, 40 or 80 mg/L under unspecified conditions for 96 hours. The concentrations provided were not specified as nominal or measured. Precipitate was observed at 40 and 80 mg/L. The mortality rate at 80 mg/L was 100%, while fish at 40 and 20 mg/L exhibited loss of equilibrium. Dark pigmentation was observed at all exposure concentrations.
96-h LC_{50} = 28.3 mg/L

Subcategory III: Ester/Phenols
Pentyl 2-hydroxybenzoate (CASRN 2050-08-0)
Zebra fish (*Danio rerio*) were exposed to pentyl 2-hydroxybenzoate at 0, 0.8, 1.1, 1.6, 2.3, 3.3 or 4.7 mg/L under static-renewal conditions for 96 hours. Test concentrations were measured by GC prior to and after 24 hours for 2 days. Precipitate was noted at the two highest concentrations (3.3 and 4.7 mg/L). No mortalities were seen at concentrations ≤ 3.3 mg/L, while 4.7 mg/L produced 100% mortality at 48 hours. Sluggish swimming was observed in fish at 2.3 and 3.3 mg/L.
96-h LC_{50} = 1.34 mg/L

Benzyl 2-hydroxybenzoate (CASRN 118-58-1)
Zebra fish (*Danio rerio*) were exposed to benzyl 2-hydroxybenzoate at 0, 0.7, 1.0, 1.4, 2.0 or 2.8 mg/L under static-renewal conditions for 96 hours. Test concentrations were measured by GC prior to and after 24 hours for 2 days. Mortalities were noted at 2.0 and 2.8 mg/L. Fish at these concentrations exhibited normal swimming behavior. No effects were seen at concentrations ≤ 1.4 mg/L.
96-h LC_{50} = 0.55 mg/L

Subcategory IV: Aldehyde/Phenol
m-Methoxy-p-hydroxybenzaldehyde (CASRN 121-33-5)
(1) Fathead minnows (*Pimephales promelas*) (20/concentration) were exposed to *m*-methoxy-*p*-hydroxybenzaldehyde (reagent-grade) in a covered non-renewal static nominal 96-hour test. Temperatures ranging were from 18-22^o Celsius. Fish were 4 to 8 weeks old and length varied from 1.1 to 3.1 cm. Various concentrations (generally by a factor of 10 or more) were conducted before conducting a definitive test. DO was ≤ 4.0 mg/L. Additional critical study details were added to the existing robust summary to enhance data quality. ECOSAR v.1.00a was used to support the evaluation of CASRN 121-33-5.
96-h LC_{50} = 116 mg/L
96-h LC_{50} = 23 mg/L (estimated)

(2) Fathead minnows (*Pimephales promelas*) (20/concentration) were exposed to *m*-methoxy-*p*-hydroxybenzaldehyde (reagent-grade) in a covered non-renewal static nominal 96-hour test. Temperatures ranging were from 18-22^o Celsius. Fish were 4 to 8 weeks old and length varied from 1.1 to 3.1 cm. Various concentrations (generally by a factor of 10 or more) were conducted before conducting a definitive test. DO was ≤ 4.0 mg/L. Additional critical study details were added to the existing robust summary to enhance data quality. ECOSAR v.1.00a was used to support the evaluation of CASRN 121-33-5.
96-h LC_{50} = 112 mg/L
96-h LC_{50} = 23 mg/L (estimated)

(3) Fathead minnows (*Pimephales promelas*) (20/concentration) were exposed to *m*-methoxy-*p*-hydroxybenzaldehyde (reagent-grade) in a covered non-renewal static nominal 96-hour test. Temperatures ranging were from 18-22^o Celsius. Fish were 4 to 8 weeks old and length varied from 1.1 to 3.1 cm. Various concentrations (generally by a factor of 10 or more) were conducted before conducting a definitive test. DO was ≤ 4.0 mg/L. Additional critical study details were added to the existing robust summary to enhance data quality.
96-h LC_{50} = 88 mg/L

(4) See fish toxicity data at (http://www.chem.unep.ch/irptc/sids/OECDSIDS/121335.pdf)

Acute Toxicity to Aquatic Invertebrates

Subcategory I: Aldehydes
p-Methoxybenzaldehyde (CASRN 123-11-5)
See aquatic invertebrate toxicity data at
http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=624478ca-b163-434a-8b6c-bae2cfa08e0c&idx=0).

Subcategory II: Esters
Methyl benzoate (CASRN 93-58-3)
Water fleas (*Daphnia magna*) were exposed to methyl benzoate at nominal concentrations of 0 (solvent and freshwater controls), 9.38, 18.8, 37.5, 75, 150 or 300 mg/L under unspecified conditions for 48 hours. Measured concentrations were not provided. At concentrations ≥ 37.5, up to 75% of daphnia were found dead or immobilized. Precipitate was observed at these higher concentrations initially, but was no longer seen following 24 hours. ECOSAR v.1.00a was used to support the evaluation of CASRN 93-58-3.
48-h EC_{50} = 32.1 mg/L
48-h EC_{50} = 28.5 mg/L (estimated)

Subcategory III: Ester/Phenols
Pentyl 2-hydroxybenzoate (CASRN 2050-08-0)
Water fleas (*Daphnia magna*) were exposed to pentyl 2-hydroxybenzoate at nominal concentrations of 0.5, 1.0, 2.0 or 4.0 mg/L. The EC_{50} is provided in the submitted test plan, but not in the robust summary. ECOSAR v.1.00a was used to support the evaluation of CASRN 2050-8-0.
48-h EC_{50} = 2.8 mg/L

48-h EC_{50} = 1.42 and 0.38 mg/L for ester and phenol moieties, respectively (estimated)

Subcategory IV: Aldehyde/Phenol
No adequate data are available for this endpoint.

Toxicity to Aquatic Plants

Subcategory I: Aldehydes
Toxicity to aquatic plants endpoint was available through SIDS and obtained from: CASRN 123-11-5 [SIAP is only available; SIAR/robust summaries are not done] (http://webnet.oecd.org/hpv/UI/SIDS_Details.aspx?Key=624478ca-b163-434a-8b6c-bae2cfa08e0c&idx=0).

Subcategory II: Esters
No data are available for this endpoint.

Subcategory III: Ester/Phenols
No data are available for this endpoint.

Subcategory IV: Aldehyde/Phenol
No data are available for this endpoint.

Sub-Chronic Toxicity to Fish

Subcategory I: Aldehydes
Benzaldehyde (CASRN 100-52-7)
Guppies (*Poecilia reticulata*) were exposed to benzaldehyde at a minimum of five concentrations (unspecified) under semi-static conditions for 14 days. A control group was exposed to the carrier solvent, acetone. The 14-day LC_{50} was calculated to be 1.57 μmol (equivalent to 0.167 mg/L)
14-day LC_{50} = 0.167 mg/L

Subcategory II: Esters
Benzyl Acetate (CASRN 140-11-4)
Larval Japanese medakas (*Oryzias latipes*) were exposed to benzyl acetate at unspecified concentrations for 28 days. The estimated maximum acceptable toxicant level was 0.92 – 1.92 mg/L. Survival was significantly ($p < 0.05$) decreased at ≥ 1.92 mg/L. The NOEC was calculated from the geometric mean of the estimated MATC.
NOEC = 1.33 mg/L

Conclusions:
Subcategory I: Aldehydes
The 96-h LC_{50} value for fish to CASRN 100-52-7 is 7.61 mg/L. The 96-h LC_{50} value for fish to CASRN 123-11-5 is 40 mg/L. The 48-h EC_{50} value for aquatic invertebrate to CASRN 123-11-5 is 45 mg/L. The 72-h EC_{50} values for aquatic plants to CASRN 123-11-5 are 61 and 59 mg/L for growth rate and biomass, respectively.

Subcategory II: Esters
The 96-h LC_{50} values for fish to CASRNs 140-11-4, 120-51-4 and 93-58-3 range from 1.34 to 28.3 mg/L. The 48-h EC_{50} value for aquatic invertebrate to CASRN 93-58-3 is 32.1 mg/L.

Subcategory III: Ester/Phenols
The 96-h LC_{50} values for fish to CASRNs 2050-08-0 and 118-58-1 are 1.34 and 0.55 mg/L, respectively. The 48-h EC_{50} value for aquatic invertebrate to CASRN 2050-08-0 is 2.8 mg/L.

Subcategory IV: Aldehyde/Phenol
The 96-h LC_{50} value for fish to CASRN 121-33-5 is 53.0 mg/L.

Table 6. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Aquatic Toxicity Data

Endpoints	*Subcategory I: Aldehydes*		*Subcategory II: Esters*				*Subcategory III: Ester/Phenols*			*Subcategory IV: Aldehyde/Phenol*
	Benzaldehyde (100-52-7)	***p*-Methoxy-benzaldehyde (123-11-5)**	**Benzyl acetate (140-11-4)**	**Benzyl benzoate (120-51-4)**	**Methyl benzoate (93-58-3)**	**Methyl *p*-methyl-benzoate (99-75-2)**	**Methyl 2-hydroxy benzoate (119-36-8)**	**Pentyl 2-hydroxy benzoate (2050-08-0)**	**Benzyl 2-hydroxy benzoate (118-58-1)**	***m*-Methoxy-*p*-hydroxy-benzaldehyde (121-33-5)**
Fish 96-h LC_{50} (mg/L)	**7.61**	**40**	**4.0**	**1.34**	**28.3**	No Data 1.34 – 28.3 (RA)	No Data 0.55 – 1.34 (RA)	**1.34**	**0.55**	**53**
Aquatic Invertebrates 48-h EC_{50} (mg/L)	No Adequate Data 45 (RA)	**45**	No Data 32.1 (RA)	No Data 32.1 (RA)	**32.1**	No Data 32.1 (RA)	No Data 2.8 (RA)	**2.8**	No Data 2.8 (RA)	No Adequate Data
Aquatic Plants 72-h EC_{50} (mg/L) Growth rate Biomass	No Data 61 59 (RA)	**61** **59**	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Chronic Toxicity to Invertebrates 21-d EC_{50} (mg/L)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	No Data	No Data	N/A

bold = measured data (i.e., derived from testing); (RA) = Read Across; N/A = not applicable, chronic testing is not warranted based on log Kow

5. Reference

Brook LT, Call DJ, Geiger, DL, and Northcott, CE editors, 1984. "Acute toxicities of organic chemicals to fathead minnows (*Pimephales promelas*)". Center for Lake Superior Environmental Studies University of Wisconsin-Superior. Supported by the US Environmental Protection Agency Through Cooperative Agreements 806864 and 809234