SCREENING-LEVEL HAZARD CHARACTERIZATION

Mixed Xylenols Category

SPONSORED CHEMICALS

2,5-Xylenol	**CASRN 95-87-4**
3,4-Xylenol	**CASRN 95-65-8**
2,4-Xylenol	**CASRN 105-67-9**
3,5-Xylenol	**CASRN 108-68-9**
2,3-Xylenol	**CASRN 526-75-0**
2,6-Xylenol	**CASRN 576-26-1**
Mixed Xylenols	**CASRN 1300-71-6**

SUPPORTING CHEMICAL

Mixed xylenols test mixture No CASRN

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

[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.

Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT's focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

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

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

Chemical Abstract Service Registry Number (CASRN)	**Sponsored Chemicals** **95-87-4** **95-65-8** **105-67-9** **108-68-9** **526-75-0** **576-26-1** **1300-71-6** **Supporting Chemical** **No CASRN**
Chemical Abstract Index Name	**Sponsored Chemicals** **Phenol, 2,5-dimethyl-** **Phenol, 3,4-dimethyl-** **Phenol, 2,4-dimethyl-** **Phenol, 3,5-dimethyl-** **Phenol, 2,3-dimethyl-** **Phenol, 2,6-dimethyl-** **Phenol, dimethyl-**
Structural Formula	**See Section 1**

Summary

The mixed xylenol category consists of six isomeric members that are solids with high water solubility and moderate vapor pressure. All members of the mixed xylenols category are expected to have moderate mobility in soil. Volatilization is considered moderate based on their Henry's Law constants. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered moderate. The mixed xylenols are expected to have low persistence (P1) and low bioaccumulation potential (B1).

Human Health Hazard

Subcategory I: Isomers of Xylenol

The acute oral toxicity of the subcategory I members is low in mice and ranges from low to moderate in rats. The acute dermal toxicity is ranges from low to moderate in rats and is moderate in rabbits. A 90-day oral gavage repeated-dose toxicity study in rats administered CASRN 105-67-9, showed decreases in body weight and hyperkeratosis and epithelial hyperplasia of the forestomach at 180 mg/kg-day; the NOAEL for systemic toxicity is 60 mg/kg-day. The subcategory I members have moderate vapor pressure and therefore, a 10 day inhalation study was included in this hazard characterization. A 10-day inhalation repeated-dose

toxicity study in rats administered CASRN 576-26-1, showed decreases in body weight at 0.2 mg/L/day; the NOAEL is 0.067 mg/L/day. There are no specific reproductive toxicity studies available for the subcategory I members; however, no adverse effects were observed on the reproductive organs in the 90-day repeated-dose toxicity study in mice or rats with CASRN 105-67-9. In an oral gavage prenatal developmental toxicity study in rats administered CASRN 576-26-1, decreased body weight gain was observed in the dams at $\geq$ 180 mg/kg-day; the NOAEL is 60 mg/kg-day. In the same study, reduced fetal body weight was observed in the pups at 540 mg/kg-day (highest dose tested); the NOAEL is 180 mg/kg-day. CASRN 105-67-9 was weakly mutagenic in bacteria *in vitro*. CASRN 576-26-1 was not mutagenic in bacteria *in vitro* and did not induce chromosomal aberrations in rats *in vivo*. Subcategory I members are irritating to rabbit and guinea pig skin and are irritating to rabbit eyes.

No data gaps were identified under the HPV Challenge Program.

Subcategory II: Commercial Mixed Xylenols

The acute toxicity of CASRN 1300-71-6 is moderate for the oral route and low for the dermal route. There were no repeated-dose/reproductive/developmental toxicity studies and no gene mutation or chromosomal aberration studies available for CASRN 1300-71-6. CASRN 1300-71-6 is irritating to rabbit skin and eyes.

Repeated-dose/reproductive/developmental toxicity, genetic toxicity (gene mutations and chromosomal aberrations) endpoints were identified as data gaps under the HPV Challenge Program.

Hazard to the Environment

For the mixed xylenols category, the sponsored chemicals were not sub-categorized for ecological purposes based on their physical and chemical properties.

The 96-h LC_{50} for fish exposed to the mixed xylenols category members ranges from 12 mg/L (CASRN 576-26-1) to 22 mg/L (CASRN 108-68-9). The 48-h EC_{50} for aquatic invertebrates ranges from 7.7 mg/L (mixed xylenols test mixture) to 11.2 mg/L (CASRN 576-26-1). The 72-h EC_{50} for aquatic plants from exposure to the supporting chemical, mixed xylenols test mixture, is 14 mg/L for biomass and is >22 mg/L for growth rate.

No data gaps were identified under the HPV Challenge Program.

The sponsor, Merisol USA LLC, submitted a Test Plan and Robust Summaries to EPA for the mixed xylenols category on July 29, 2002. EPA posted the submission on the ChemRTK HPV challenge website on August 16, 2002 (http://www.epa.gov/oppt/chemrtk/pubs/summaries/mxylcat/c13884tc.htm). EPA comments on the original submission were posted to the website on January 15, 2003. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on May 12, 2003 and May 5, 2006, which were posted to the ChemRTK website on June 11, 2003 and July 21, 2006, respectively.

Category Justification

The mixed xylenols category consists of the six structural isomers of xylenol which are 2,5-xylenol, 3,4-xylenol, 2,4-xylenol, 3,5-xylenol, 2,3-xylenol, 2,6-xylenol and a commercial mixed xylenols mixture. These isomers are grouped together based on similarities in structure and physicochemical properties. The xylenol isomers have the same molecular weight and the same substituent groups (two methyl and one hydroxyl) surrounding a benzene ring. They differ only in the position of the two methyl groups on the ring. The Sponsor has indicated that the commercial mixed xylenols mixture is not compositionally defined, but contains, at most, 22.5% xylenol; the rest of the mixture is a combination of phenol, cresols, xylenols, ethylphenols and higher boiling alkyl phenols. Based on their structural similarity, estimated and measured physicochemical properties and environmental fate data for all six xylenol isomers, grouping these isomers in this proposed category is supported. Submission of hydrolysis testing results was not believed to be necessary.

To address the human health endpoints, EPA divided the category into two subcategories: Subcategory I consists of the six individual xylenol isomers and Subcategory II consists of the commercial mixed xylenols mixture. For the aquatic toxicity endpoints, similarities in the available acute fish and invertebrate toxicity data for the different isomers supports their grouping into a single category. In addition, the chemical structures and physical chemical properties of the compounds that make up the mixed xylenols commercial mixture (CASRN 1300-71-6) suggest that the phenols, cresols and ethylphenolic compounds found in this mixture will not have significantly different aquatic toxicity and can therefore, be grouped with the individual xylenol isomers.

Supporting Chemical Justification

In the original test plan, the sponsor proposed testing for an equimolar mixture of the six xylenol isomers to satisfy data gaps for the individual xylenol isomers. EPA commented that the sponsor should test a commercially available composition of xylenols representative of xylenol mixtures that would be most likely to contribute to significant human exposure. The sponsor noted that the commercial product, WES 297, which contains all six xylenol isomers, has the highest percentage of xylenols (22.5%) of any of the commercial mixtures. The sponsor developed a test mixture (referred to as mixed xylenols test mixture) that contains portions of the six xylenol isomers normalized to match the ratios of xylenol isomers occurring in commercial product WES 297. The test mixture contains the following six isomers at Mole percentages listed in parentheses: 2,5-xylenol (16.4%); 3,4-xylenol (16.9%); 2,4-xylenol (22.7%); 3,5-xylenol

(11.1%); 2,3-xylenol (18.2%) and 2,6-xylenol (14.7%). EPA notes, however, that the results for the 100% mixed xylenol test mixture tested by the sponsor is not representative of the toxicity of the commercial mixtures to which people may be exposed since the commercial mixtures contain, at most, 22.5% xylenol; the rest of the mixture is a combination of phenol, cresols, xylenols, ethylphenols and higher boiling alkyl phenols. Therefore the mixed xylenols test mixture cannot be used for read-across purposes to the sponsored chemical, CASRN 1300-71-6, mixed xylenol, in this hazard characterization for human health purposes. Saturation and competition for metabolism that may occur with the administration of the xylenols test mixture would likely lead to an underestimation of toxicity from the individual isomers and therefore, the mixed xylenols test mixture cannot be used to read-across to the individual isomers for human health endpoints. As a result, this information is not included in the hazard characterization.

EPA does not agree that health effects data from cresols (*o*-cresol, *m*-cresol, *p*-cresol and an *m/p*-cresol mixture) can be used to support the mixed xylenols category and this information has not been included in the hazard characterization. EPA has determined that for human health, the supporting chemical cannot be used for read-across purposes for either the six xylenol isomers in Subcategory I or for CASRN 1300-71-6 (the sponsored substance known as mixed xylenols). For aquatic toxicity, the category members have not been separated into subcategories and the supporting chemical, mixed xylenols test mixture (No CASRN) can be used for read-across purposes to the xylenol isomers as well as to the mixed xylenols commercial mixture.

1. Chemical Identity

1.1 Identification and Purity

The following description is taken from the 2001 Test Plan and Robust Summary: Xylenols are isomeric forms of dimethyl phenol containing two methyl groups attached to the ortho, meta, or para positions of the phenol ring. There are six possible isomeric forms. The purity of CASRN 576-26-1 was >98% when specified in the Robust Summaries. Test substance purity for the other CASRNs was not specified in the Robust Summary.

The chemical structures of the mixed xylenols are depicted in Table 1.

Table 1. Mixed Xylenols Category Sponsored Chemical Structures

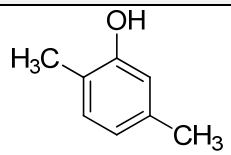
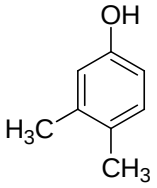
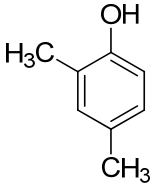
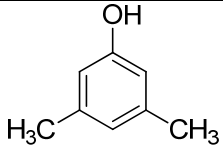
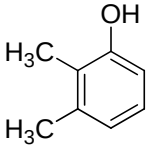
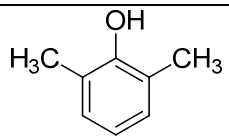
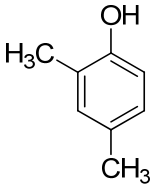
Chemical Name	CASRN	Structure
Phenol, 2,5-dimethyl-	95-87-4	

Table 1. Mixed Xylenols Category Sponsored Chemical Structures

Chemical Name	CASRN	Structure
Phenol, 3,4-dimethyl-	95-65-8	
Phenol, 2,4-dimethyl-	105-67-9	
Phenol, 3,5-dimethyl-	108-68-9	
Phenol, 2,3-dimethyl-	526-75-0	
Phenol, 2,6-dimethyl-	576-26-1	
Phenol, dimethyl-	1300-71-6	 Representative structure[1]

[1] The sponsor indicates that no commercial product is specifically assigned to the CASRN 1300-71-6, referred to as "mixed xylenols" or phenol, dimethyl-, nor is there a defined mixture associated with this substance. Therefore, the sponsor defined "mixed xylenols" by utilizing the known molar % of a related product (xylenols WES 297) which contains all of the six sponsored xylenols. The commercial mixture, xylenols WES 297, contains 16.4 mol% phenol, 2,5-dimethyl-, 16.9 mol% phenol, 3,4-dimethy-l, 22.7 mol% phenol, 2,4-dimethyl-(representative isomer), 11.1 mol % phenol, 3,5-dimethyl-, 18.2 mol% phenol, 2,3-dimethyl-, 14.7 mol% phenol, 2-6-dimethyl-.
The representative structure shown is phenol, 2,4-dimethyl-as it is present at the highest concentration in the mixture according to the sponsor.

1.2 Physical-Chemical Properties

The physical-chemical properties of the mixed xylenols category are summarized in Table 2.

Table 2. Physical-Chemical Properties of the Mixed Xylenols Category[1]

Property	Phenol, 2,3-dimethyl- Value	Phenol, 2,4-dimethyl- Value	Phenol, 2,5-dimethyl- Value	Phenol, 2,6-dimethyl- Value	Phenol, 3,4-dimethyl- Value	Phenol, 3,5-dimethyl- Value	Phenol, dimethyl-[2] Value
CASRN	526-75-0	105-67-9	95-87-4	576-26-1	95-65-8	108-68-9	1300-71-6
Molecular Weight	122.17	122.17	122.17	122.17	122.17	122.17	122.17
Physical State	Solid[3]	Solid[3]	Solid[3]	Solid[3]	Solid[3]	Solid[3]	Solid[3]
Melting Point	72.6°C (measured) 72.8°C (measured)[3]	24.5°C (measured)	74.8°C (measured)	45.6°C (measured)	65.1°C (measured)	63.4°C (measured)	24.5°C (measured, for typical phenol, 2,4-dimethyl-)
Boiling Point	216.9°C (measured)	211.0°C (measured)	211.2°C (measured)	201.1°C (measured)	227.0°C (measured)	221.7°C (measured)	211.0°C (measured, for typical phenol, 2,4-dimethyl-)
Vapor Pressure	0.09 mm Hg at 25°C (measured)	0.10 mm Hg at 25°C (measured)[4]	0.16 mm Hg at 25°C (measured)	0.27 mm Hg at 25°C (measured)	0.04 mm Hg at 25°C (measured)	0.04 mm Hg at 25°C (measured)	0.10 mm Hg at 25°C (measured, for typical phenol, 2,4-dimethyl-)[4]
Water Solubility	4,750 mg/L at 25°C (measured)	7,870 mg/L at 25°C (measured)	3,540 mg/L at 25°C (measured)	6,050 mg/L at 25°C (measured)	4,760 mg/L at 25°C (measured)	4,880 mg/L at 25°C (measured)	7,870 mg/L at 25°C (measured, for typical phenol, 2,4-dimethyl-)
Dissociation Constant (pK_a)	pK_a = 10.54 (measured)[5]	pK_a = 10.60 (measured)[5]	pK_a = 10.41 (measured)[5]	pK_a = 10.62 (measured)[5]	pK_a = 10.36 (measured)[5]	pK_a = 10.19 (measured)[5]	pK_a = 10.60 (measured, for typical phenol, 2,4-dimethyl-)[5]
Henry's Law Constant	7.38×10^{-7} atm-m^3/mole (measured)[5]	9.51×10^{-7} atm-m^3/mole (measured)[5]	1.12×10^{-6} atm-m^3/mole (measured)[5]	6.65×10^{-6} atm-m^3/mole (measured)[5]	4.15×10^{-7} atm-m^3/mole (measured)[5]	6.14×10^{-7} atm-m^3/mole (measured)[5]	9.51×10^{-7} atm-m^3/mole (measured, for typical phenol, 2,4-dimethyl-[5]
Log Kow	2.42 (measured)	2.36 (measured)	2.36 (measured)	2.36 (measured)	2.33 (measured)	2.35 (measured)	2.36 (measured, for typical phenol, 2,4-dimethyl-)

1 Merisol USA, LLC. 2003. Revised Test Plan and Robust Summary for the Mixed Xylenols Category. Available online at http://www.epa.gov/hpv/pubs/summaries/mxylcat/c13884tc.htm as of June 30, 2010.
2 The sponsor indicates that no commercial product is specifically assigned to the CASRN 1300-71-6, referred to as "mixed xylenols" or phenol, dimethyl-, nor is there a defined mixture associated with this substance. Therefore, the sponsor defined "mixed xylenols" by utilizing the known molar % of a related product (xylenols WES 297) which contains all of the six sponsored xylenols. The commercial mixture, xylenols WES 297, contains 16.4 mol% phenol, 2,5-dimethyl-, 16.9 mol% phenol, 3,4-dimethy-l, 22.7 mol% phenol, 2,4-dimethyl-(representative isomer), 11.1 mol% phenol, 3,5-dimethyl-, 18.2 mol% phenol, 2,3-dimethyl-, 14.7 mol% phenol, 2-6-dimethyl-.
3 Lide, DR. 2008. CRC Handbook of Chemistry and Physics 89th ed. CRC Press.
4 Daubert, TE; Danner, RP. 1989. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, DC: Taylor and Francis.
5 SRC. 2010. The Physical Properties Database (PHYSPROP). SRC: Syracuse, NY. Available online at http://www.srcinc.com/what-we-do/free-demos.aspx as of June 30, 2010.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

The mixed xylenols category chemicals had an aggregated production and/or import volume in the United States between 105 million pounds and 550 million pounds in calendar year 2005.

- CASRN 95-65-8: 1 to <10 million pounds;
- CASRN 95-87-4: 1 to <10 million pounds;
- CASRN 105-67-9: 1 to <10 million pounds;
- CASRN 108-68-9: 1 to <10 million pounds;
- CASRN 526-75-0: 1 to <10 million pounds;
- CASRN 576-26-1: 100 to <500 million pounds;

CASRN 1300-71-6 was not reported in the 2006 IUR.

CASRN 95-65-8, 95-87-4, 105-67-9, 108-68-9, 526-75-0 and 576-26-1:
Non-confidential industrial processing and uses, and commercial and consumer use information for these chemicals were claimed not readily obtainable (NRO).

2.2 Environmental Exposure and Fate

The environmental fate properties are provided in Table 3. The xylenol isomers of the mixed xylenols category are expected to have moderate mobility in soil. Biodegradation data indicate that mixed xylenols will be readily biodegradable, as all six xylenol isomers in the mixture are readily biodegradable. Using an aerobic degradation test in activated sludge in a laboratory study, the COD removal after incubation at 20°C for 5 days was between 89.3 and 97.5% for all isomers. The half-life for phenol, phenol, 2,4-dimethyl- in unacclimated soil was 3.5 days. The rates of hydrolysis are expected to be negligible since these substances do not possess labile functional groups that hydrolyze under environmental conditions. The rates of volatilization of all members are considered moderate based on their Henry's Law constants. The mixed xylenols are expected to have low persistence (P1) and low bioaccumulation potential (B1).

Table 3. Environmental Fate Characteristics of the Mixed Xylenols Category[1]

Property	Phenol, 2,3-dimethyl-	Phenol, 2,4-dimethyl-	Phenol, 2,5-dimethyl-	Phenol, 2,6-dimethyl-	Phenol, 3,4-dimethyl-	Phenol, 3,5-dimethyl-	Phenol, dimethyl-[2]
	Value	**Value**	**Value**	**Value**	**Value**	**Value**	**Value**
CASRN	526-75-0	105-67-9	95-87-4	576-26-1	95-65-8	108-68-9	1300-71-6
Photodegradation Half-life	4.8 hours (measured)[3]	5.3 hours (measured)[3]	4.8 hours (measured)[3]	5.8 hours (measured)[3]	4.7 hours (measured)[3]	3.4 hours (measured)[3]	5.3 hours (measured)[3]
Hydrolysis Half-life	Stable	Stable	Stable	Stable	Stable	Stable	Stable

Table 3. Environmental Fate Characteristics of the Mixed Xylenols Category[1]

Property	Phenol, 2,3-dimethyl-	Phenol, 2,4-dimethyl-	Phenol, 2,5-dimethyl-	Phenol, 2,6-dimethyl-	Phenol, 3,4-dimethyl-	Phenol, 3,5-dimethyl-	Phenol, dimethyl-[2]
	Value	Value	Value	Value	Value	Value	Value
Biodegradation	95.5% in 5 days (readily biodegradable)[4]	Half-life = 3.5 days (readily biodegradable); 94.5% in 5 days (readily biodegradable)[4]	94.5% in 5 days (readily biodegradable)[4]	94.3% in 5 days (readily biodegradable)[4]	97.5% in 5 days (readily biodegradable)[4]	89.3% after 5 days (readily biodegradable)[4]	Half-life = 3.5 days (readily biodegradable); 94.5% in 5 days (readily biodegradable)[4]
Bioaccumulation Factor	BAF = 16.9 (estimated)[5]	BCF = 15.1–151 (measured)[6] BAF = 12.3 (estimated)[5]	BAF = 13 (estimated)[5]	BAF = 13.7 (estimated)[5]	BAF = 10.9 (estimated)[5]	BAF = 13.5 (estimated)[5]	BCF = 15.1–151 (measured)[6] BAF = 12.3 (estimated)[5]
Log K_{oc}	2.7 (estimated)[5]	2.02–2.08 (measured)[7] 2.7 (estimated)[5]	2.7 (estimated)[5]	2.7 (estimated)[5]	2.7 (estimated)[5]	2.3–3.1 (measured)[8]	2.02–2.08 (measured)[7] 2.7 (estimated)[5]
Fugacity (Level III Model)[5]							
Air (%)	0.3	0.3	0.3	0.4	0.3	0.3	0.4
Water (%)	25.1	25.2	25.2	25.0	25.0	25.2	25.2
Soil (%)	74.1	74.0	74.0	74.1	74.2	74.1	74.0
Sediment (%)	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Persistence[9]	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)
Bioaccumulation[9]	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)

[1] Merisol USA, LLC. 2003. Revised Test Plan and Robust Summary for the Mixed Xylenols Category. Available online at http://www.epa.gov/hpv/pubs/summaries/mxylcat/c13884tc.htm as of June 30, 2010.

[2] The sponsor indicates that no commercial product is specifically assigned to the CASRN 1300-71-6, referred to as "mixed xylenols" or phenol, dimethyl-, nor is there a defined mixture associated with this substance. Therefore, the sponsor defined "mixed xylenols" by utilizing the known molar % of a related product (xylenols WES 297) which contains all of the six sponsored xylenols. The commercial mixture, xylenols WES 297, contains 16.4 mol% phenol, 2,5-dimethyl-, 16.9 mol% phenol, 3,4-dimethy-l, 22.7 mol% phenol, 2,4-dimethyl-(representative isomer), 11.1 mol% phenol, 3,5-dimethyl-, 18.2 mol% phenol, 2,3-dimethyl-, 14.7 mol% phenol, 2-6-dimethyl-.

[3] Atkinson, R. 1994. Journal of Physical and Chemical Reference Data Monograph No. 2. Gas-Phase Trophoshperic Chemistry or Organic Compounds. Woodbury, NY: American Chemical Society and the American Institute of Physics for the National Institute of Standards and Technology, 245 pp.

[4] Pitter, P. 1976. Determination of biological degradability of organic substances. Water Res 10(3):231–235.

[5] U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online at http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm as of July 6, 2010.

[6] Shiu, WY; Ma, KC; Varhanickova, D; Mackay, D. 1994. Chlorophenols and alkylphenols: A review and correlation of environmentally relevant properties and fate in an evaluative environment. Chemosphere 29(6):1155–1224.

[7] Kopinke, FD; Poerschmann, J; Stottmeister, U. 1995. Sorption of organic pollutants on anthropogenic human matter. Environ Sci Technol 29(4):941–950.

[8] Southworth, GR; Keller JL. 1986. Hydrophobic sorption of polar organics by low organic carbon soils. Water Air Soil Poll 28(3–4):239–248.

[9] Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

Conclusion: The mixed xylenol category consists of six isomeric members that are solids with high water solubility and moderate vapor pressure. All members of the mixed xylenols category are expected to have moderate mobility in soil. Volatilization is considered moderate based on their Henry's Law constants. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered moderate. The mixed xylenols 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 4. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Oral Toxicity

Subcategory I: Isomers of Xylenol

3,4-Xylenol (CASRN 95-65-8)
Rats and mice (10/dose; strain/sex not specified) were administered 3,4-xylenol via gavage at unspecified doses between 200 and 3200 mg/kg No further experimental details were provided. TSCATS (OTS0533431).
LD_{50} (rat) = 1600 mg/kg
LD_{50} (mouse) = 400 mg/kg

The acute oral toxicity of several xylenols is reported in Ullmann's Encyclopedia of Industrial Chemistry (Fiege, 2003).
2,5-Xylenol (CASRN 95-87-4)
LD_{50} (rat) =444 mg/kg
LD_{50} (mouse) =383 mg/kg

3,5-Xylenol (CASRN 108-68-9)
LD_{50} (rat) =608 mg/kg
LD_{50} (mouse) =477 mg/kg

2,6-Xylenol (CASRN 576-26-1)
LD_{50} (rat) =296 mg/kg
LD_{50} (mouse) =450 mg/kg

Subcategory II: Commercial Mixed Xylenols

Mixed Xylenols (CASRN 1300-71-6)
Male Sprague-Dawley rats (3/dose) were administered a single dose of an undescribed xylenol mixture (Product Code 80910) via gavage at 5000 mg/kg and observed for 14 days. Two of three rats died by day 2. TSCATS (OTS0205981[288]).
LD_{50} < 5000 mg/kg

Acute Dermal Toxicity

Subcategory I: Isomers of Xylenol

The acute dermal toxicity of several xylenols is reported in Ullmann's Encyclopedia of Industrial Chemistry (Fiege, 2003).

2,4-Xylenol (CASRN 105-67-9)
LD_{50} (rat) =1040 mg/kg

3,5-Xylenol (CASRN 108-68-9)
LD_{50} (rat) =2400 mg/kg
LD_{50} (rabbit) =2000 mg/kg

2,6-Xylenol (CASRN 576-26-1)
LD_{50} (rat) =2325 mg/kg
LD_{50} (rabbit) =1000 mg/kg

Subcategory II: Commercial Mixed Xylenols

Mixed Xylenols (CASRN 1300-71-6)
Male New Zealand white rabbits (2/dose) were treated with an undescribed xylenol mixture (Product Code 80910) via dermal application at 5000 mg/kg, on shaved skin under occluded conditions for 24 hours and observed for 14 days. No mortalities were observed. TSCATS (OTS0205981[288]).
LD_{50} >5000 mg/kg

Repeated-Dose Toxicity

Subcategory I: Isomers of Xylenol

2,4-Xylenol (CASRN 105-67-9)
(1) In a 90-day study, Sprague-Dawley rats (10/sex/dose) were dosed via gavage with 2,4-xylenol (99.2% pure) in corn oil, administered at 0, 60, 180, and 540 mg/kg-day. Effects examined include mortality, clinical signs, body weights, food and water consumption, hematology and clinical chemistry, organ weights, and gross histopathology. In the high-dose group, 6 males and all of the females died. Additional animals (6 males and 6 females) were added to these groups and dosed for the full 90 days. At final sacrifice, 7 of 16 males and 3 of 16 females survived at 540 mg/kg-day. The deaths were attributed to the corrosive action of 2,4-xylenol on the esophagus and stomach. No significant clinical signs were noted in animals from the other treatment groups. Body weight was significantly decreased in females at 180 mg/kg-day and in both sexes at 540 mg/kg-day. In males, brain, kidney and testes to body weight ratios were significantly increased at 540 mg/kg-day while the thymus to body weight ratio was significantly decreased at 60 mg/kg-day. In females, kidney to body weight ratios were significantly decreased at 60 mg/kg-day and significantly increased at 180 mg/kg-day. Brain to body weight ratios were significantly increased at 180 mg/kg-day and thymus and lung to brain weight ratios were significantly decreased at 180 mg/kg-day. A statistically significant increase

in mean corpuscular volume was observed in females at 540 mg/kg-day. Clinical chemistry changes included: significantly decreased AST (males) in the 180 mg/kg-day dose group and significantly decreased phosphate (females) in the 60 mg/kg-day dose group. Hyperkeratosis and epithelial hyperplasia (of the forestomach) were observed in all of the males at ≥180 mg/kg-day and epithelial hyperplasia was observed in 60% of the females at 180 mg/kg-day and all surviving females at 540 mg/kg-day (Daniel *et al.*, 1993).
LOAEL = 180 mg/kg-day (based on decreased body weight and histopathology)
NOAEL = 60 mg/kg-day

(2) In a 90-day study, Albino mice (30/sex/dose) were dosed via gavage with 2,4-xylenol administered at 0, 5, 50, and 250 mg/kg-day. Two control groups, untreated and vehicle (corn oil) were also established. Effects examined include mortality, clinical signs, body weights, food consumption, ophthalmology, hematology and clinical chemistry, organ weights, and gross histopathology. There were no significant differences in mortality between treated and control animals. No treatment-related changes were noted in body weight, food consumption or ocular effects by 90 days post-dosing. Clinical signs observed in both genders of the high-dose group include: squinting, lethargy, prostration, and ataxia. Females treated with 250 mg/kg-day had statistically significant hematologic changes including lower mean corpuscular volume and mean corpuscular hemoglobin concentration. Significant differences were not found in gross necropsy or histopathological evaluation, or in organ weights, except for an increase in adrenal weights of females at 5 mg/kg-day.
LOAEL = 250 mg/kg-day (based on hematologic effects)
NOAEL = 50 mg/kg-day

2,6-Xylenol (CASRN 576-26-1)
(1) In a 28-day study, Wistar rats (5/sex/dose) were dosed via gavage with 2,6-xylenol in olive oil, at dose levels of 0, 20, 100, 400, and 800 mg/kg-day once daily, 5 days/week. One male rat in the highest dose group died, apparently due to a perforation of the forestomach wall. Clinical signs were observed in the two highest dose groups and included: hypothermia, ataxia, salivation, and reduced general state. Pathological effects in the 800 mg/kg-day treatment group included erosions/ulceration in the glandular stomach of some animals of both sexes at 800 mg/kg-day and decreased red blood cells, hemoglobin, and hematocrit in females at ≥400 mg/kg-day. Significantly increased absolute and relative liver weights were observed in females at ≥100 mg/kg-day and in males at ≥400 mg/kg-day. Increased extramedullary erythropoiesis in the spleen was observed in 3 males and all females at 800 mg/kg-day and 2 males and 4 females at 400 mg/kg-day. TSCATS (OTS0001264).
LOAEL = 400 mg/kg-day (based on hematological effects)
NOAEL = 100 mg/kg-day

(2) In a range-finding study, Fischer rats (10/sex/concentration) were exposed to 2,6-xylenol as an aerosol at 0, 67, 200 or 670 mg/m^3 (0, 0.067, 0.2, or 0.67 mg/L) for 5 hours/day over 10 consecutive days. All rats survived whole-body exposures to 2,6-xylenol aerosols. Hemoglobin and platelets were significantly decreased in males at 670 mg/m^3. All rats of both sexes at 670 mg/m^3 exhibited moderate squamous metaplasia of olfactory epithelium and red nasal discharge observed after treatment abated overnight. Body weights were decreased for female rats at 670 mg/m^3 and for male rats at ≥ 200 mg/m^3. Increased kidney weights (absolute and relative to

body weight) were observed for male and female rats at 670 mg/m^3. Organ-to-body-weight ratios for heart, lung and liver were elevated in female rats at 670 mg/m^3. TSCATS (OTS0527745).
LOAEL = 0.2 mg/L/day (based on decreased body weight)
NOAEL = 0.067 mg/L/day

Subcategory II: Commercial Mixed Xylenols

No data are available for this endpoint.

Reproductive Toxicity

Subcategory I: Isomers of Xylenol

There are no specific reproductive toxicity studies available for the subcategory I members; however, no adverse effects were observed on the reproductive organs in the 90-day repeated-dose toxicity study in mice or rats with CASRN 105-67-9.

Subcategory II: Commercial Mixed Xylenols

No data are available for this endpoint.

Developmental Toxicity

Subcategory I: Isomers of Xylenol

2,6-Xylenol (CASRN 576-26-1)
In a prenatal developmental toxicity study, pregnant Sprague-Dawley rats (24/dose) were exposed to 2,6-xylenol via gavage at doses of 0, 60, 180 or 540 mg/kg-day during gestation days 6 – 15. Maternal toxicity (body weight gain suppression; statistical significance not reported) was observed at ≥ 180 mg/kg-day. Maternal mortality (2/24) and reduction in fetal body weight (statistical significance not reported) occurred at 540 mg/kg-day. No information on organ weights, malformations or histopathology was provided.
LOAEL (maternal toxicity) = 180 mg/kg-day (based on decreased body weight gain)
NOAEL (maternal toxicity) = 60 mg/kg-day
LOAEL (developmental toxicity) = 540 mg/kg-day (based on reduced fetal body weight)
NOAEL (developmental toxicity) = 180 mg/kg-day

Subcategory II: Commercial Mixed Xylenols

No data are available.

Genetic Toxicity – Gene Mutation

Subcategory I: Isomers of Xylenol
In vitro

2,4-Xylenol (CASRN 105-67-9)
(1) In an NTP study, *S. typhimurium* strains TA98, TA100 and TA1535 were exposed to 2,4-xylenol at concentrations of 0, 3.3, 10, 33, 100, 333 and 500 µg/plate, in the presence and absence of metabolic activation. Positive and negative controls were tested concurrently, and responded appropriately. The test substance was weakly positive in TA100, in the presence of metabolic activation (http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=salmonella.salmonellaData&endpointlist=SA&study%5Fno=704425&cas%5Fno=105%2D67%2D9&activetab=detail).
CASRN 105-67-9 was weakly positive in this assay.

(2) In a reverse-mutation assay, *S. typhimurium* strains TA98, TA100, TA1535 and TA1537 were exposed to 2,4-xylenol at concentrations of 0, 0.33, 1.0, 3.3, 10 and 33 µg/plate, in the presence and absence of metabolic activation. Positive and negative controls were tested concurrently, and responded appropriately. No further details were provided.
CASRN 105-67-9 was not mutagenic in this assay.

2,6-Xylenol (CASRN 576-26-1)
(1) In a reverse-mutation assay, *S. typhimurium* strains TA98, TA100, TA1535 and TA1537 were exposed to 2,6-xylenol at concentrations of 0, 10, 33.3, 100, 333.3, 1000, 2500 and 5000 µg/plate, in the presence and absence of metabolic activation. No further details were provided.
CASRN 576-26-1 was not mutagenic in this assay.

(2) In a reverse-mutation assay, *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to 2,6-xylenol at concentrations of 0, 0.05, 0.15, 0.5, 1.5 and 5.0 mg/plate, in the presence and absence of metabolic activation. Positive and negative controls were tested concurrently, and responded appropriately. Cytotoxicity was not observed. No positive responses were observed with the test substance. TSCATS (OTS0534388).
CASRN 576-26-1 was not mutagenic in this assay.

Subcategory II: Commercial Mixed Xylenols

No data are available.

Genetic Toxicity – Chromosomal Aberrations

Subcategory I: Isomers of Xylenol

In vivo
2,6-Xylenol (CASRN 576-26-1)
Sprague-Dawley rats were exposed to 2,6-xylenol via gavage at 0, 350, 700 or 1400 mg/kg-day for males and at 0, 300, 600 or 1200 mg/kg-day for females. Cells were collected from treated and control animals and examined microscopically for structural and numeric chromosome aberrations after 12, 24 or 36 hours post-dosing. There were no statistically significant increases in the percentage of cells with chromosomal aberrations in any treatment group at any time point.
CASRN 576-26-1 did not induce chromosomal aberrations in this assay.

Subcategory II: Commercial Mixed Xylenols

No *in vitro* or *in vivo* data are available for this endpoint.

Additional Information

Skin Irritation

Subcategory I: Isomers of Xylenol

3,4-Xylenol (CASRN 95-65-8)
Three guinea pigs (strain/sex not reported) were administered 3,4-xylenol at concentrations of 0.25 – 1.0 mg/kg applied to the skin. No further experimental details were provided. All three exposed animals survived. Moderate edema developed within 24 hours followed by necrosis and eschar in the treated area. Summarized from TSCATS (OTS0533431).
CASRN 95-65-8 was severely irritating to guinea pig skin in this study.

3,5-Xylenol (CASRN 108-68-9)
Rabbits (number/strain/sex not specified) were exposed to undiluted 3,5-xylenol (volume not reported) applied to skin. Exposure caused hyperemia and edema with moderate necrosis. Moderate burns to the skin were observed after 5 – 10 minutes of contact. Summarized from TSCATS (OTS0517019).
CASRN 108-69-9 was severely irritating to rabbit skin in this study.

2,6 Xylenol (CASRN 576-26-1)
Rabbits (3 intact, 3 abraded; strain/sex not specified) were exposed to undiluted 2,6-xylenol at 0.5 g applied to skin. Exposure caused severe burns to skin by 72 hours following treatment.
CASRN 576-26-1 was severely irritating to rabbit skin in this study.

Subcategory II: Commercial Mixed Xylenols

Mixed xylenols (CASRN 1300-71-6)
Male New Zealand White rabbits (2/dose) were treated with an undescribed xylenol mixture (Product Code 80910) via dermal application at 5000 mg/kg (undiluted), on shaved skin under occluded conditions for 24 hours and observed for 14 days. Exposure caused severe erythema, severe edema and eschar formation. TSCATS (OTS0205981[288]).
CASRN 1300-71-6 was severely irritating to rabbit skin in this study.

Eye Irritation

Subcategory I: Isomers of Xylenol

3,4-Xylenol (CASRN 95-65-8)
Rabbits were exposed to 3,4-xylenol in the conjunctival sac of one eye (undiluted). Exposure caused moderate but permanent eye injury. TSCATS (OTS0533431).
CASRN 95-65-8 was moderately irritating to rabbit eyes in this study.

3,5-Xylenol (CASRN 108-68-9)
Rabbits (number/strain/sex not specified) were exposed to 3,5-xylenol in the conjunctival sac of one eye (volume not reported; undiluted and 10% solution in propylene glycol) in range-finding studies. Exposure caused severe conjunctival injury and corneal damage sufficient to cause some permanent impairment of vision. TSCATS (OTS0517019).
CASRN 108-68-9 was severely irritating to rabbit eyes in this study.

2,6-Xylenol (CASRN 576-26-1)
Rabbits (n=6; strain/sex not specified) were instilled with 0.1 g of 2,6-xylenol into the conjunctival sac of one eye. Exposure caused severe irritation, corneal opacity, corneal sloughing and corneal damage in test animals by 72 hours following treatment.
***CASRN 576-26-1* was severely irritating to rabbit eyes in this study.**

Subcategory II: Commercial Mixed Xylenols

Mixed xylenols (CASRN 1300-71-6)
Male New Zealand White rabbits (2/dose) were instilled with 0.1 mL of an undescribed xylenol mixture (Product Code 80910; undiluted) in the conjunctival sac of one eye in range-finding studies. Exposure caused moderate conjunctival injury. TSCATS (OTS0205981[288]).
CASRN 1300-71-6 was moderately irritating to rabbit eyes in this study.

Conclusion:

Subcategory I: Isomers of Xylenol
The acute oral toxicity of the subcategory I members is low in mice and ranges from low to moderate in rats. The acute dermal toxicity is ranges from low to moderate in rats and is moderate in rabbits. A 90-day oral gavage repeated-dose toxicity study in rats administered CASRN 105-67-9, showed decreases in body weight and hyperkeratosis and epithelial hyperplasia of the forestomach at 180 mg/kg-day; the NOAEL for systemic toxicity is 60 mg/kg-day. The subcategory I members have moderate vapor pressure and therefore, a 10 day inhalation study was included in this hazard characterization. A 10-day inhalation repeated-dose toxicity study in rats administered CASRN 576-26-1, showed decreases in body weight at 0.2 mg/L/day; the NOAEL is 0.067 mg/L/day. There are no specific reproductive toxicity studies available for the subcategory I members; however, no adverse effects were observed on the reproductive organs in the 90-day repeated-dose toxicity study in mice or rats with CASRN 105-67-9. In an oral gavage prenatal developmental toxicity study in rats administered CASRN 576-26-1, decreased body weight gain was observed in the dams at $\geq$ 180 mg/kg-day; the NOAEL is 60 mg/kg-day. In the same study, reduced fetal body weight was observed in the pups at 540 mg/kg-day (highest dose tested); the NOAEL is 180 mg/kg-day. CASRN 105-67-9 was weakly mutagenic in bacteria *in vitro*. CASRN 576-26-1 was not mutagenic in bacteria *in vitro* and did not induce chromosomal aberrations in rats *in vivo*. Subcategory I members are irritating to rabbit and guinea pig skin and are irritating to rabbit eyes.

Subcategory II: Commercial Mixed Xylenols

The acute toxicity of CASRN 1300-71-6 is moderate for the oral route and low for the dermal route. There were no repeated-dose/reproductive/developmental toxicity studies and no gene mutation or chromosomal aberration studies available for CASRN 1300-71-6. CASRN 1300-71-6 is irritating to rabbit skin and eyes.

Table 4. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data

	Subcategory I						Subcategory II
Endpoints	**SPONSORED CHEMICAL 2,5-Xylenol (95-87-4)**	**SPONSORED CHEMICAL 3,4-Xylenol (95-65-8)**	**SPONSORED CHEMICAL 2,4-Xylenol (105-67-9)**	**SPONSORED CHEMICAL 3,5-Xylenol (108-68-9)**	**SPONSORED CHEMICAL 2,3-Xylenol (526-75-0)**	**SPONSORED CHEMICAL 2,6-Xylenol (576-26-1)**	**SPONSORED CHEMICAL Mixed xylenols (1300-71-6)**
Acute Oral Toxicity LD_{50} (mg/kg)	**444 (rat)** **383 (mouse)**	**1600 (rat)** **400 (mouse)**	No Adequate Data 296 (RA)	**608 (rat)** **477 (mouse)**	No Adequate Data 296 (RA)	**296 (rat)** **450 (mouse)**	**< 5000[a] (rat)**
Acute Dermal Toxicity LD_{50} (mg/kg)	No Data 1040 (RA)	No Data 1040 (RA)	**1040 (rat)**	**2400 (rat)** **2000 (rabbit)**	No Data 1040 (RA)	**2325 (rat)** **1000 (rabbit)**	**>5000 (rabbit)**
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-day)	No Data NOAEL =60 LOAEL = 180 (RA) No Data NOAEL =50 LOAEL = 250 (RA)	No Data NOAEL =60 LOAEL = 180 (RA) No Data NOAEL =50 LOAEL = 250 (RA)	**(90-day, rat)** **NOAEL =60** **LOAEL = 180** **(90-day, mouse)** **NOAEL =50** **LOAEL = 250**	No Data NOAEL =60 LOAEL = 180 (RA) No Data NOAEL =50 LOAEL = 250 (RA)	No Data NOAEL =60 LOAEL = 180 (RA) No Data NOAEL =50 LOAEL = 250 (RA)	**(28-day, rat)** **NOAEL =100** **LOAEL = 400** No Data NOAEL =50 LOAEL = 250 (RA)	Data gap[b]
Repeated-Dose Toxicity NOAEL/LOAEL Inhalation (mg/L/day)	No Data NOAEL =0.0 67 LOAEL = 0.2 (RA)	No Data NOAEL = 0.067 LOAEL = 0.2 (RA)	No Data NOAEL = 0.067 LOAEL = 0.2 (RA)	No Data NOAEL = 0.067 LOAEL = 0.2 (RA)	No Data NOAEL = 0.067 LOAEL = 0.2 (RA)	**(rat)** **NOAEL = 0.067** **LOAEL = 0.2**	Data gap[b]
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg-day)	There are no specific reproductive toxicity studies available for the subcategory I members; however, no adverse effects were observed on the reproductive organs in the 90-day repeated-dose toxicity study in mice or rats with CASRN 105-67-9.						Data gap[b]

Table 4. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data

	Subcategory I						Subcategory II
Endpoints	**SPONSORED CHEMICAL 2,5-Xylenol (95-87-4)**	**SPONSORED CHEMICAL 3,4-Xylenol (95-65-8)**	**SPONSORED CHEMICAL 2,4-Xylenol (105-67-9)**	**SPONSORED CHEMICAL 3,5-Xylenol (108-68-9)**	**SPONSORED CHEMICAL 2,3-Xylenol (526-75-0)**	**SPONSORED CHEMICAL 2,6-Xylenol (576-26-1)**	**SPONSORED CHEMICAL Mixed xylenols (1300-71-6)**
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-day)							
Maternal Toxicity	No Data NOAEL= 60 LOAEL= 180	No Data NOAEL= 60 LOAEL= 180	No Data NOAEL= 60 LOAEL= 180	No Data NOAEL= 60 LOAEL= 180	No Data NOAEL= 60 LOAEL= 180	**(rat) NOAEL= 60 LOAEL= 180**	Data gap[b]
Developmental Toxicity	NOAEL = 180 LOAEL = 540 (RA)	NOAEL = 180 LOAEL = 540 (RA)	NOAEL = 180 LOAEL = 540 (RA)	NOAEL = 180 LOAEL = 540 (RA)	NOAEL = 180 LOAEL = 540 (RA)	**NOAEL = 180 LOAEL = 540**	
Genetic Toxicity – Gene Mutation *In vitro*	No Data Negative (RA)	No Data Negative (RA)	**Weakly positive**	No Data Negative (RA)	No Data Negative (RA)	**Negative**	Data gap[b]
Genetic Toxicity – Chromosomal Aberrations *In vitro*	—						Data gap[b]
Genetic Toxicity – Chromosomal Aberrations *In vivo*	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	**Negative**	—
Additional Information							
Eye Irritation	—	—	—	**(rabbit) Severely irritating**	—	**(rabbit) Severely irritating**	**(rabbit)[a] Moderately irritating**
Skin Irritation	—	**(guinea pig) Severely irritating**	—	**(rabbit) Severely irritating**	—	**(rabbit) Severely irritating**	**(rabbit)[a] Severely irritating**

Measured data in bold text; (RA) = Read Across; **—** indicates that endpoint was not assessed for this substance.

[a] Identified as Produce Code 80910, with unspecified isomers and concentrations.

[b] Mixed xylenols represents commercial mixtures containing varying ratios of two or more xylenol isomers as well as varying percentages of other component chemicals, including phenol, cresols and ethylphenols. The mixed xylenols test mixture (supporting chemical) cannot be used for read-across purposes to the Subcategory II mixed xylenols sponsored chemical since the test mixture contains only xylenol isomers in the absence of other phenolics that would be required for it to provide adequate support for the commercial product(s).

4. Hazard to the Environment

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 5. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Toxicity to Fish

3,4-Xylenol (CASRN 95-65-8)
Fathead minnows (*Pimephales promelas*) were exposed to 3,4-xylenol at unspecified concentrations under static conditions for 96 hours.
96-h LC_{50} = 14 mg/L

2,4-Xylenol (CASRN 105-67-9)
Fathead minnows (*Pimephales promelas*) were exposed to CASRN 105-67-9 at measured concentrations of 0, 5.2, 8.6, 14.4, 24 and 40 mg/L under flow-through conditions for 96 hours. Water quality, fish behavior, pharmacotoxic signs, body weight and survival were measured during the exposure period.
96-h LC_{50} = 16.6 mg/L

3,5-Xylenol (CASRN 108-68-9)
Goldfish (*Carassius auratus*) were treated with CASRN 108-68-9 at unspecified measured concentrations and levels equivalent to LC_{50} (TLm) were estimated at 96 hours.
96-h LC_{50} = 22 mg/L

2,6-Xylenol (CASRN 576-26-1)
(1) Fathead minnow (*Pimephales promelas*) were exposed to CASRN 576-26-1 at unspecified concentrations under flow-through conditions for 8 days. Water quality, fish behavior, pharmacotoxic signs, body weight and survival were measured during the exposure period, including 96 hours and 8 days post-treatment.
96-h LC_{50} > 27 mg/L

(2) Winter flounder (*Pseudopleuronectes americanus*) were exposed to CASRN 576-26-1 at nominal concentrations of 0, 3.75, 7.5, 15, 30 and 60 mg/L seawater under static, unaerated conditions for 4 days. Survival was measured at four periods during the exposure period from 24 to 96 hours post-treatment.
96-h LC_{50} = 12 mg/L

Acute Toxicity to Aquatic Invertebrates

2,6-Xylenol (CASRN 576-26-1)
Water fleas (*Daphnia magna*) were exposed to CASRN 576-26-1 at unspecified concentrations under static conditions for 48 hours. .
48-h EC_{50} = 11.2 mg/L

Mixed xylenols test mixture (consists of CASRN 95-87-4, 95-65-8, 105-67-9, 108-68-9, 526-75-0, 576-26-1; supporting chemical)
Water fleas (*Daphnia magna*) were exposed to a xylenol mixture, including the following six isomers at Mole percentages listed in parentheses: CASRN 95-87-4 (16.4%); CASRN 95-65-8 (16.9%); CASRN 105-67-9 (22.7%); CASRN 108-68-9 (11.1%); CASRN 526-75-0 (18.2%) and CASRN 526-26-1 (14.7%). Measured test concentrations in a static closed system were 0, 2.0, 5.4, 11, 21 and 47 mg/L. The initial pH was 8 and temperatures were 19 – 21 °C. Each of five treatment levels (negative control, solvent, three analytical QC control groups) included four replicate vessels with five daphnids each. Water quality measurements included: specific conductance = 500 µmhos/cm; total hardness (as $CaCO_3$) = 190 mg/L and alkalinity (as $CaCO_3$) = 120 mg/L. Preliminary testing indicated that volatilization of mixed xylenols test mixture could be controlled with closed test vessels. The 48-hour growth rate NOEC was 5.4 mg/L.
48-h EC_{50} = 7.7 mg/L

Toxicity to Aquatic Plants

Mixed xylenols test mixture (consists of CASRN 95-87-4, 95-65-8, 105-67-9, 108-68-9, 526-75-0, 576-26-1; supporting chemical)
Freshwater green algae (*Psuedokirchneriella subcapitata*) were exposed to a xylenol mixture, including the following six isomers at Mole percentages listed in parentheses: CASRN 95-87-4 (16.4%); CASRN 95-65-8 (16.9%); CASRN 105-67-9 (22.7%); CASRN 108-68-9 (11.1%); CASRN 526-75-0 (18.2%) and CASRN 526-26-1 (14.7%) Mean measured concentrations were 0, 1.7, 3.1, 6.3, 13 and 25 mg/L under static conditions for 72 hours. The closed system was operated at 22 – 24 °C, with continuous illumination at 7,000 – 8,600 lux and shaking at 100 rpm. The pH was 8.2 at the beginning of the study and 8.9 – 9.5 at 72 hours post-treatment. Cell numbers were measured at 24, 48 and 72 hours. The 72-hour NOEC value was 1.7 mg/L for biomass and growth rate.
EC_{50} (total biomass) = 14 mg/L
EC_{50} (growth rate) > 22 mg/L

Conclusion: The 96-h LC_{50} for fish exposed to the mixed xylenols category members ranges from 12 mg/L (CASRN 576-26-1) to 22 mg/L (CASRN 108-68-9). The 48-h EC_{50} for aquatic invertebrates ranges from 7.7 mg/L (mixed xylenols test mixture) to 11.2 mg/L (CASRN 576-26-1). The 72-h EC_{50} for aquatic plants from exposure to the supporting chemical, mixed xylenols test mixture, is 14 mg/L for biomass and is >22 mg/L for growth rate.

5. References

Daniel, F. B., Robinson, M., Olson, G. R., York, R. G., and Condie, L. W. 1993. Ten and ninety-day toxicity studies of 2,4-dimethylphenol in Sprague-Dawley rats. *Drug and Chemical Toxicology* **16**, 351-368.

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

Endpoints	SPONSORED CHEMICAL 2,5-Xylenol (95-87-4)	SPONSORED CHEMICAL 3,4-Xylenol (95-65-8)	SPONSORED CHEMICAL 2,4-Xylenol (105-67-9)	SPONSORED CHEMICAL 3,5-Xylenol (108-68-9)	SPONSORED CHEMICAL 2,3-Xylenol (526-75-0)	SPONSORED CHEMICAL 2,6-Xylenol (576-26-1)	SPONSORED CHEMICAL Mixed xylenols (1300-71-6)[a]	SUPPORTING CHEMICAL Mixed xylenols test mixture (no CASRN)[b]
Fish 96-h LC_{50} (mg/L)	No Adequate Data 12 (RA)	**14**	**16.6**	**22**	No Data 12 (RA)	**12**	No Data 12 (RA)	–
Aquatic Invertebrates 48-h EC_{50} (mg/L)	No Adequate Data 7.7 (RA)	No Data 7.7 (RA)	No Adequate Data 7.7 (RA)	No Data 7.7 (RA)	No Adequate Data 7.7 (RA)	**11.2**	No Data 7.7 (RA)	**7.7**
Aquatic Plants 72-h EC_{50} (mg/L) (biomass) **(growth rate)**	No Data 14 (RA)	No Data 14 (RA)	No Data 14 (RA)	No Data 14 (RA)	No Data 14 (RA)	No Data 14 (RA)	No Data 14 (RA)	. **14** **> 22**

bold = measured data (i.e., derived from testing); (RA) = Read Across; – indicates that endpoint was not assessed for this substance

[a]Mixed xylenols represent commercial mixtures containing varying ratios of two or more xylenol isomers as well as varying percentages of other component chemicals, including phenol, cresols and ethylphenols.

[b]Mixed xylenols test mixture includes the following six isomers at Mole percentages listed in parentheses: 2,5-xylenol (16.4%); 3,4-xylenol (16.9%); 2,4-xylenol (22.7%); 3,5-xylenol (11.1%); 2,3-xylenol (18.2%) and 2,6-xylenol (14.7%).