

## **SCREENING-LEVEL HAZARD CHARACTERIZATION**

### **Mononitrile Category**

#### **SPONSORED CHEMICALS**

**(See Section 1)**

#### **SUPPORTING CHEMICALS**

**(See Section 1)**

The High Production Volume (HPV) Challenge Program<sup>1</sup> 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<sup>1,2</sup>) 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<sup>2,3</sup> 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

---

<sup>1</sup> U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

<sup>2</sup> U.S. EPA. HPV Challenge Program – Information Sources; <http://www.epa.gov/chemrtk/pubs/general/guidocs.htm>.

<sup>3</sup> 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.

<p><b>Chemical Abstract Service Registry Number (CASRN)</b></p>	<p><b><u>Sponsored Chemicals</u></b>  <b>16529-56-9</b>  <b>13284-42-9</b>  <b>25899-50-7</b>  <b>26294-98-4</b>  <b>4635-87-4</b>  <b>16545-78-1</b>  <b>16529-66-1</b>  <b>592-51-8</b></p> <p><b><u>Supporting Chemicals</u></b>  <b>109-75-1</b>  <b>107-13-1</b></p>
<p><b>Chemical Abstract Index Name</b></p>	<p><b><u>Sponsored Chemicals</u></b>  <b>3-Butenenitrile, 2-methyl-</b>  <b>2-Pentenenitrile</b>  <b>2-Pentenenitrile, (2Z)-</b>  <b>2-Pentenenitrile, (2E)-</b>  <b>3-Pentenenitrile</b>  <b>3-Pentenenitrile, (3Z)-</b>  <b>3-Pentenenitrile, (3E)-</b>  <b>4-Pentenenitrile</b></p> <p><b><u>Supporting Chemicals</u></b>  <b>3-Butenenitrile</b>  <b>2-Propenenitrile</b></p>
<p><b>Formula</b></p>	<p><b>See Section 1</b></p>
<p style="text-align: center;"><b>Summary</b></p> <p>The mononitrile category consists of linear straight and branched chain alkene members with a common nitrile functional group at one end of the parent alkene chain. The cis- and trans-isomers of CASRN 13284-42-9 and CASRN 4635-87-4 are also included in the mononitrile category. All eight members are liquids with high water solubility and high vapor pressure. All members are expected to possess high mobility in soil. Volatilization of the members is considered moderate based on estimated Henry's Law constants. Measured hydrolysis data is not available; however, nitriles may be susceptible to hydrolysis. The rate of atmospheric photooxidation is considered moderate to rapid. All members in this mononitrile category are expected to have moderate persistence (P2) and low bioaccumulation potential (B1).</p>	

The acute toxicity of mononitrile category members is moderate via the oral route and moderate to high via the dermal and inhalation routes. In a 29-day oral repeated-dose toxicity study in rats, CASRN 25899-50-7 showed decreased bodyweight and atrophy of nasal dorsal olfactory mucosa at 10 mg/kg-bw/day. Female rats showed reduction in forelimb and hindlimb grip strength at this dose; the NOAEL for systemic toxicity was not established. Repeated inhalation exposure of rats for 28 days to ~ 0.1 mg/L/day CASRN 25899-50-7 showed decreased male body weights, changes in sorbitol dehydrogenase activity and microscopic nasal lesions in rats; the NOAEL for systemic toxicity was ~ 0.01 mg/L/day. No data were submitted for the reproductive/developmental toxicity endpoints. Mononitrile category members induced gene mutations in bacteria and mammalian cells *in vitro*, and induced chromosomal aberrations *in vitro*. Mononitrile category members are not irritating to rabbit or guinea pig skin; however, they do cause eye irritation in rabbits. Mononitrile category members are not skin sensitizers.

The 96-hr LC<sub>50</sub> value for the supporting chemical, CASRN 109-75-1, to fish, is 182 mg/L. The 96-hr LC<sub>50</sub> value for the supporting chemical, CASRN 107-13-1, to fish, is 9.3 -18.1 mg/L and the 48-hr EC/LC<sub>50</sub> value to aquatic invertebrates is 7.6-8.7 mg/L. The 30-day chronic toxicity value of the supporting chemical, CASRN 107-13-1, to fish, is 2.6 mg/L and the 21-day chronic value for aquatic invertebrates is 0.71 mg/L.

The reproductive/developmental toxicity and toxicity to aquatic plants endpoints were identified as data gaps under the HPV Challenge Program.

The sponsor, E.I. du Pont de Nemours and Co., submitted a Test Plan and Robust Summaries to EPA for the mononitrile category on November 12, 2002. EPA posted the submission on the ChemRTK HPV Challenge website on December 20, 2002 (<http://www.epa.gov/oppt/chemrtk/pubs/summaries/mononitr/c14094tc.htm>). EPA comments on the original submission were posted to the website on April 22, 2003. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on January 6, 2003 and February 12, 2004, which were posted to the ChemRTK website on March 20, 2003 and April 21, 2004, respectively.

The sponsored chemical has since been purchased by another company (INVISTA Chemical). Post-submission testing was performed by INVISTA Chemical and, at the time of this posting [September, 2010], some robust summaries/test results have not yet been received by EPA.

### **Category Justification**

The mononitriles category is composed of linear or branched alkenyl nitriles having the double bond at the 2-, 3- or 4- position. According to the sponsor, the terminal nitrile group and limited chain length of each category member suggest that the eight isomers (including the *cis*- and *trans*- isomers of both 2- and 3-pentenenitrile) should have similar physicochemical, environmental and toxicological properties. EPA agrees that the measured and estimated values provided for physical-chemical properties, environmental fate and health effects generally support this conclusion.

In the case of aquatic toxicity, EPA considers vinyl nitriles to be the most toxic chemicals in the category compared with allylic nitriles or with 4-pentenenitrile and used the toxicity data for vinyl nitriles as an anchor to evaluate this category.

### **Justification for Supporting Chemicals**

The two supporting chemicals are only used to support the aquatic, not human health, toxicity endpoints. The sponsor provided data for acrylonitrile (2-propenenitrile) and 3-butenitrile in support of the aquatic toxicity endpoints of 2-pentenenitrile and 3-pentenenitrile, respectively. Acrylonitrile is similar to 2-pentenenitrile in that it has a vinylic cyanide and contains two less carbon atoms. 3-Butenenitrile is similar to 3-pentenenitrile in that it has an allylic cyanide and contains one less carbon atom. These similarities support the use of these substances as supporting chemicals.

## **1. Chemical Identity**

### **1.1 Identification and Purity**

The test plan states that the mononitriles are liquids. The purity, when given, varied between 37% and 100%.

Table 1 includes structures of the mononitriles and supporting chemicals included in the category.

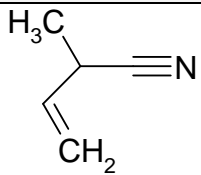
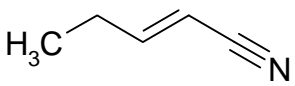
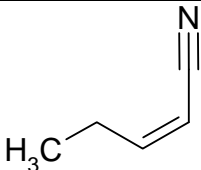
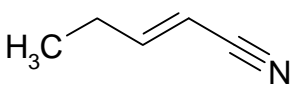
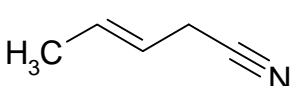
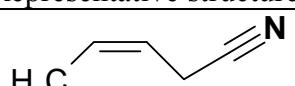
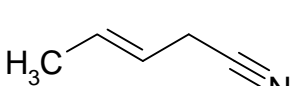
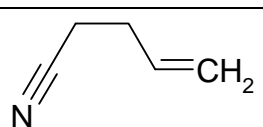
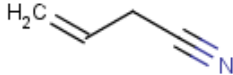
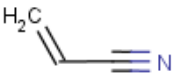
Table 1. Chemical Structures for Mononitriles		
Chemical Name	CASRN	Structure
<b>SPONSORED CHEMICAL</b>		
3-Butenenitrile, 2-methyl-	16529-56-9	
2-Pentenenitrile	13284-42-9	 Representative structure <sup>1</sup>
2-Pentenenitrile, (2Z)-	25899-50-7	
2-Pentenenitrile, (2E)-	26294-98-4	
3-Pentenenitrile	4635-87-4	 Representative structure <sup>1</sup>
3-Pentenenitrile, (3Z)-	16545-78-1	
3-Pentenenitrile, (3E)-	16529-66-1	
4-Pentenenitrile	592-51-8	

Table 1. Chemical Structures for Mononitriles		
Chemical Name	CASRN	Structure
<b>SUPPORTING CHEMICAL</b>		
3-Butenenitrile	109-75-1	
2-propenenitrile (Acrylonitrile)	107-13-1	

<sup>1</sup>The sponsor indicates that 2-pentenenitrile and 3-pentenenitrile are composed of mixtures of their respective cis- and trans-isomers

## 1.2 Physical-Chemical Properties

The physical-chemical properties are summarized in Tables 2 and 3.

The members of the mononitrile category are liquids with high water solubility and high vapor pressure. 2-Pentenenitrile and 3-pentenenitrile are composed of mixtures of their respective cis- and trans-isomers.

Property	<b>3-Butenenitrile, 2-methyl-</b>	<b>2-Pentenenitrile<sup>2</sup></b>	<b>2-Pentenenitrile, (2Z)-</b>	<b>2-Pentenenitrile, (2E)-</b>
	Value	Value	Value	Value
CASRN	16529-56-9	13284-42-9	25899-50-7	26294-98-4
Molecular Weight	81.12	81.12	81.12	81.12
Physical State	Clear liquid	Colorless liquid	Colorless liquid <sup>3</sup>	Colorless liquid <sup>3</sup>
Melting Point	<25°C <sup>4</sup>	<25°C <sup>4</sup>	<25°C <sup>4</sup>	<25°C <sup>4</sup>
Boiling Point	121–145°C with decomposition (measured)	127°C (measured)	127–128°C at 766 mm Hg (measured) <sup>5</sup>	144.7–147.9°C at 746 mm Hg (measured) <sup>6</sup>
Vapor Pressure	6.4–18.2 mm Hg at 25°C (estimated) <sup>7</sup>	14.1 mm Hg at 25°C (estimated) <sup>7</sup>	14.0–14.1 mm Hg at 25°C (estimated) <sup>7</sup>	5.6– 6.5 mm Hg at 25°C (estimated) <sup>7</sup>
Water Solubility	6,917 mg/L (measured)	7,472 mg/L (measured)	7,472 mg/L (measured)	7,472 mg/L (measured)
Dissociation Constant (pK <sub>a</sub> )	Not applicable	Not applicable	Not applicable	Not applicable
Henry's Law Constant	5.33×10 <sup>-5</sup> atm-m <sup>3</sup> /mol (estimated) <sup>8</sup>	2.28×10 <sup>-4</sup> atm-m <sup>3</sup> /mol (estimated) <sup>8</sup>	2.28×10 <sup>-4</sup> atm-m <sup>3</sup> /mol (estimated) <sup>8</sup>	2.28×10 <sup>-4</sup> atm-m <sup>3</sup> /mol (estimated) <sup>8</sup>
Log K <sub>ow</sub>	1.12 (estimated) <sup>8</sup>	1.11 (estimated) <sup>8</sup>	1.11 (estimated) <sup>8</sup>	1.11 (estimated) <sup>8</sup>

<sup>1</sup> DuPont. 2004. Revised Test Plan and Robust Summary for the Mononitrile Category. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/mononitr/c14094tc.htm> as of July 7, 2010.

<sup>2</sup> Measured data presented is for the mixture of cis- and trans-isomers of 2-pentenenitrile.

<sup>3</sup> Data estimated based on structural similarities between 2-pentenenitrile, 2-pentenenitrile, (2E)- and 2-pentenenitrile, (2Z)-.

<sup>4</sup> Estimated based on the physical state of the compound and an analog, 1-pentanenitrile (CASRN 110-59-8), which has a melting point of -96°C.

<sup>5</sup> Aldrich Chemical Company. 2002. Aldrich Handbook of Fine Chemicals and Laboratory Equipment 2003–2004. Milwaukee, WI: Aldrich Chem Co. p. 1422.

<sup>6</sup> Beilstein literature search.

<sup>7</sup> NOMO5. 1987. Programs to Enhance PC-Gems Estimates of Physical Properties for Organic Compounds. The Mitre Corp.

<sup>8</sup> 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/episuitedi.htm> as of July 7, 2010.

<b>Property</b>	<b>3-Pentenenitrile<sup>2</sup></b>	<b>3-Pentenenitrile, (3Z)-</b>	<b>3-Pentenenitrile, (3E)-</b>	<b>4-Pentenenitrile</b>
	<b>Value</b>	<b>Value</b>	<b>Value</b>	<b>Value</b>
CASRN	4635-87-4	16545-78-1	16529-66-1	592-51-8
Molecular Weight	81.12	81.12	81.12	81.12
Physical State	Colorless to amber liquid	Colorless to amber liquid <sup>3</sup>	Colorless to amber liquid <sup>3</sup>	Liquid
Melting Point	<25°C <sup>4</sup>	<25°C <sup>4</sup>	<25°C <sup>4</sup>	<25°C <sup>4</sup>
Boiling Point	144–147°C with decomposition (measured)	144°C (measured)	144–147°C (measured) <sup>5</sup>	140°C (measured) <sup>5</sup>
Vapor Pressure	5.9–6.7 mm Hg at 25°C (estimated) <sup>6</sup>	6.7 mm Hg at 25°C (estimated) <sup>6</sup>	24.9 mm Hg at 50°C (measured) <sup>5</sup> ; 5.9– 6.7 mm Hg at 25°C (estimated) <sup>6</sup>	8.0 mm Hg at 25°C (estimated) <sup>6</sup>
Water Solubility	7,924 mg/L (measured)	7,924 mg/L (measured)	7,924 mg/L (measured)	6,794 mg/L (estimated) <sup>7</sup>
Dissociation Constant (pK <sub>a</sub> )	Not applicable	Not applicable	Not applicable	Not applicable
Henry's Law Constant	6.29×10 <sup>-5</sup> atm-m <sup>3</sup> /mol (estimated) <sup>7</sup>	6.29×10 <sup>-5</sup> atm-m <sup>3</sup> /mol (estimated) <sup>7</sup>	6.29×10 <sup>-5</sup> atm-m <sup>3</sup> /mol (estimated) <sup>7</sup>	2.39×10 <sup>-5</sup> atm-m <sup>3</sup> /mol (estimated) <sup>7</sup>
Log K <sub>ow</sub>	1.11 (estimated) <sup>7</sup>	1.11 (estimated) <sup>7</sup>	1.11 (estimated) <sup>7</sup>	1.19 (estimated) <sup>7</sup>

<sup>1</sup> DuPont. 2004. Revised Test Plan and Robust Summary for the Mononitrile Category. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/mononitr/c14094tc.htm> as of July 7, 2010.

<sup>2</sup> Measured data presented is for the mixture of cis- and trans-isomers of 3-pentenenitrile.

<sup>3</sup> Data estimated based on structural similarities between 3-pentenenitrile, 3-pentenenitrile, (3E)- and 3-pentenenitrile, (3Z)-.

<sup>4</sup> Estimated based on the physical state of the compound and an analog, 1-pentenenitrile (CASRN 110-59-8), which has a melting point of -96°C.

<sup>5</sup> Aldrich Chemical Company. 2009. Aldrich Handbook of Fine Chemicals and Laboratory Equipment 2009–2010. Milwaukee, WI: Aldrich Chem Co. p. 2077.

<sup>6</sup> NOMOS. 1987. Programs to Enhance PC-Gems Estimates of Physical Properties for Organic Compounds.

<sup>7</sup> 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/episuitdl.htm> as of July 7, 2010.

## **2. General Information on Exposure**

### **2.1 Production Volume and Use Pattern**

The Mononitrile category chemicals had an aggregated production and/or import volume in the United States between 602 million pounds and one billion 520 million pounds in calendar year 2005.

- CASRN 592-51-8: 1 to <10 million pounds;
- CASRN 4635-87-4 : 500 million to <1 billion pounds;
- CASRN 16529-56-9 : 100 to <500 million pounds;
- CASRN 25899-50-7: 1 to <10 million pounds;

CASRN 13284-42-9, 16529-66-1, 16545-78-1 and 26294-98-4 were not reported in the 2006 IUR.

CASRN 592-51-8, 4635-87-4 and 16529-56-9:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemicals include other basic organic chemical manufacturing as intermediates. No commercial and consumer uses were reported.

CASRN 25899-50-7:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing and pharmaceutical and medicine manufacturing as intermediates. No commercial and consumer uses were reported.

## 2.2 Environmental Exposure and Fate

The environmental fate properties of the mononitrile category are summarized in Tables 4 and 5.

All eight members of the mononitrile category are expected to possess high mobility in soil. A non-GLP compliant OECD Guideline 301B (Modified Sturm) test, in which biodegradability is measured as CO<sub>2</sub> evolution, found 3-pentenenitrile, 3-butenitrile, 2-methyl- and 2-pentenenitrile, (2Z)- to be not readily biodegradable, with degradation rates of 21% in 28 days, 8% in 21 days, and 3% in 28 days, respectively. Biodegradability of 2-pentenenitrile; 2-pentenenitrile, (2E)-; 3-pentenenitrile, (3E)-; 3-pentenenitrile, (3Z)-; and 4-pentenenitrile was determined using a read-across approach from the experimental biodegradation (not readily biodegradable) results, based on structural similarities. Measured hydrolysis data are not available; however, nitriles may be susceptible to hydrolysis. The rate of volatilization of all members is considered to be moderate based on estimated Henry's Law constants. All mononitrile category members are expected to have moderate persistence (P2) and low bioaccumulation potential (B1).

<b>Property</b>	<b>3-Butenenitrile, 2-methyl-</b>	<b>2-Pentenenitrile</b>	<b>2-Pentenenitrile, (2Z)-</b>	<b>2-Pentenenitrile, (2E)-</b>
	<b>Value</b>	<b>Value</b>	<b>Value</b>	<b>Value</b>
CASRN	16529-56-9	13284-42-9	25899-50-7	26294-98-4
Photodegradation Half-life	4.8 hours (estimated) <sup>2</sup>	11.3–12.7 hours (estimated) <sup>2</sup>	12.7 hours (estimated) <sup>2</sup>	11.3 hours (estimated) <sup>2</sup>
Hydrolysis Half- life	No data	No data	No data	No data
Biodegradation	8% after 21 days (not readily biodegradable)	No data	3% after 28 days (not readily biodegradable)	No data
Bioaccumulation Factor	BAF = 2.04 (estimated) <sup>2</sup>	BAF = 2.09 (estimated) <sup>2</sup>	BAF = 2.09 (estimated) <sup>2</sup>	BAF = 2.09 (estimated) <sup>2</sup>
Log K <sub>oc</sub>	1.40 (estimated) <sup>2</sup>	1.45 (estimated) <sup>2</sup>	1.45 (estimated) <sup>2</sup>	1.45 (estimated) <sup>2</sup>
Fugacity (Level III Model) <sup>2</sup>				
Air (%)	1.2	6.0	6.0	6.0
Water (%)	34.6	35.3	35.3	35.3
Soil (%)	64.1	58.5	58.5	58.5
Sediment (%)	<0.1	0.1	0.1	0.1
Persistence <sup>3</sup>	P2 (moderate)	P2 (moderate)	P2 (moderate)	P2 (moderate)
Bioaccumulation <sup>3</sup>	B1 (low)	B1 (low)	B1 (low)	B1 (low)

<sup>1</sup> DuPont. 2004. Revised Test Plan and Robust Summary for the Mononitrile Category. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/mononitr/c14094tc.htm> as of July 7, 2010.

<sup>2</sup> 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/episuitedi.htm> as of July 8, 2010.

<sup>3</sup> Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

<b>Property</b>	<b>3-Butenenitrile, 2-methyl-</b>	<b>2-Pentenenitrile</b>	<b>2-Pentenenitrile, (2Z)-</b>	<b>2-Pentenenitrile, (2E)-</b>
	<b>Value</b>	<b>Value</b>	<b>Value</b>	<b>Value</b>
CASRN	16529-56-9	13284-42-9	25899-50-7	26294-98-4
Photodegradation Half-life	4.8 hours (estimated) <sup>2</sup>	11.3–12.7 hours (estimated) <sup>2</sup>	12.7 hours (estimated) <sup>2</sup>	11.3 hours (estimated) <sup>2</sup>
Hydrolysis Half- life	No data	No data	No data	No data
Biodegradation	8% after 21 days (not readily biodegradable)	No data	3% after 28 days (not readily biodegradable)	No data
Bioaccumulation Factor	BAF = 2.04 (estimated) <sup>2</sup>	BAF = 2.09 (estimated) <sup>2</sup>	BAF = 2.09 (estimated) <sup>2</sup>	BAF = 2.09 (estimated) <sup>2</sup>
Log K <sub>oc</sub>	1.40 (estimated) <sup>2</sup>	1.45 (estimated) <sup>2</sup>	1.45 (estimated) <sup>2</sup>	1.45 (estimated) <sup>2</sup>
Fugacity (Level III Model) <sup>2</sup>				
Air (%)	1.2	6.0	6.0	6.0
Water (%)	34.6	35.3	35.3	35.3
Soil (%)	64.1	58.5	58.5	58.5
Sediment (%)	<0.1	0.1	0.1	0.1
Persistence <sup>3</sup>	P2 (moderate)	P2 (moderate)	P2 (moderate)	P2 (moderate)
Bioaccumulation <sup>3</sup>	B1 (low)	B1 (low)	B1 (low)	B1 (low)

<sup>1</sup> DuPont. 2004. Revised Test Plan and Robust Summary for the Mononitrile Category. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/mononitr/c14094tc.htm> as of July 7, 2010.

<sup>2</sup> 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 8, 2010.

<sup>3</sup> 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 mononitrile category consists of linear straight and branched chain alkene members with a common nitrile functional group at one end of the parent alkene chain. The cis- and trans-isomers of 2-pentenenitrile and 3-pentenenitrile are also included in the mononitrile category. All eight members are liquids with high water solubility and high vapor pressure. All members are expected to possess high mobility in soil. Volatilization of the members is considered moderate based on estimated Henry's Law constants. Measured hydrolysis data is not available; however, nitriles may be susceptible to hydrolysis. The rate of atmospheric photooxidation is considered moderate to rapid. All members in this mononitrile category are expected to have moderate persistence (P2) and low bioaccumulation potential (B1).

### 3. Human Health Hazard

A summary of health effects data submitted for SIDS endpoints is provided in Table 6. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

#### *Acute Oral Toxicity*

##### ***2-Methyl-3-butenitrile (CASRN 16529-56-9)***

ChR-CD male rats (1/dose) were administered CASRN 16529-56-9 (dispersed in peanut oil) via gavage at 200, 300, 450, 670, 1000, 1500, 2250 or 5000 mg/kg-bw and observed for 14 days following dosing. Mortality occurred at  $\geq 1000$  mg/kg-bw.

**Approximate Lethal Dose = 1000 mg/kg-bw**

##### ***cis-2-Pentenenitrile (CASRN 25899-50-7)***

(1) Male Crl:CD rats (1/dose) were administered CASRN 25899-50-7 (dispersed in corn oil) via gavage at 130, 200, 300, 450, 670, 1000 or 2300 mg/kg-bw and observed for 14 days following dosing. Mortality occurred at doses of  $\geq 450$  mg/kg-bw.

**Approximate Lethal Dose = 450 mg/kg-bw**

(2) Female Sprague-Dawley rats (4/dose) were administered CASRN 25899-50-7 via gavage at 31, 63, 125 or 250 mg/kg-bw followed by 14 days observation. One survivor was reported for the high-dose group. This study is a TSCATS submission (OTS0537162; 8EHQ-0492-3057).

**LD<sub>50</sub> > 125 < 250 mg/kg-bw**

##### ***3-Pentenenitrile (CASRN 4635-87-4)***

Male ChR-CD rats (1/dose) were administered CASRN 4635-87-4 via gavage at 90, 130, 200, 300, 450, 670, 2250 or 5000 mg/kg-bw and observed for 14 days following dosing. Mortality occurred at doses of  $\geq 300$  mg/kg-bw.

**Approximate Lethal Dose = 300 mg/kg-bw**

##### ***4-Pentenenitrile (CASRN 592-51-8)***

ChR-CD male rats (1/dose) were administered CASRN 592-51-8 via gavage at 200, 300, 450, 670, 1000, 1500, 2250 or 5000 mg/kg-bw and observed for 14 days following dosing. Mortality occurred at  $\geq 2250$  mg/kg-bw.

**Approximate Lethal Dose = 2250 mg/kg-bw**

#### *Acute Inhalation Toxicity*

##### ***2-Methyl-3-butenitrile (CASRN 16529-56-9)***

ChR-CD male rats (6/concentration) were exposed to CASRN 16529-56-9 as a vapor at nominal concentrations of 815, 1060, 1540, 1812, 2416, 2870, 3200 or 3835 ppm (~ 2.7, 3.5, 5.1, 6.0, 8.0, 9.5, 11 and 13 mg/L, respectively) for 4 hours and observed for 14 days following exposure.

Lethality occurred at  $\geq 2416$  ppm (~ 8.0 mg/L).

**LC<sub>50</sub> ~ 10 mg/L**

***2-Pentenenitrile (CASRN 13284-42-9)***

Rats (5/sex/concentration; strain not specified) were exposed to CASRN 13284-42-9 vapor at concentrations of 20, 120, 560, 790 or 1000 ppm (~ 0.06, 0.40, 1.6, 2.6 and 3.3 mg/L, respectively) for 4 hours and observed for 14 – 28 days following exposure. Lethality occurred at  $\geq$  790 ppm (2.6 mg/L). The LC<sub>50</sub> for this study was 740 ppm. This study is a TSCATS submission (OTS0529919; 8EHQ-1190-1121).

**LC<sub>50</sub> ~ 2.4 mg/L**

***cis-2-Pentenenitrile (CASRN 25899-50-7)***

CrI:CD®BR rats (5/sex/concentration) were exposed nose-only to CASRN 25899-50-7 vapor at mean total concentrations of 18, 140, 650, 900 or 1200 ppm (~ 0.06, 0.46, 2.2, 3.0 and 4.0 mg/L, respectively) followed by a 14- or 28-day observation period. Lethality occurred at 900 and 1200 ppm (~ 3.0 and 4.0 mg/L, respectively) and the LC<sub>50</sub> was determined to be 850 ppm. **LC<sub>50</sub> ~ 2.81 mg/L**

***3-Pentenenitrile (CASRN 4635-87-4)***

ChR-CD male rats (6/concentration) were exposed to CASRN 4635-87-4 as a vapor at nominal concentrations of 338, 359, 447, 538 or 692 ppm (~ 1.12, 1.19, 1.48, 1.78 and 2.30 mg/L, respectively) for 4 hours and observed for 14 days following exposure. Mortalities were observed at  $\geq$  359 ppm (~ 1.19 mg/L). The LC<sub>50</sub> was determined to be 420 ppm.

**LC<sub>50</sub> ~ 1.39 mg/L**

***4-Pentenenitrile (CASRN 592-51-8)***

ChR-CD male rats (6/concentration) were exposed to CASRN 592-51-8 as a vapor at nominal concentrations of 616, 1308, 2084, 2265, 2948, 3292 or 4606 ppm (~ 2.04, 4.34, 6.91, 7.51, 9.78, 10.9 and 15.2 mg/L, respectively) for 4 hours and observed for 14 days following exposure. Mortalities were observed at  $\geq$  2265 ppm (~ 7.51 mg/L).

**LC<sub>50</sub> ~ 8.46 mg/L**

***Acute Dermal Toxicity***

***2-Methyl-3-butenitrile (CASRN 16529-56-9)***

New Zealand White rabbits (6 males/dose) were administered a mixture containing 2-methyl-3-butenitrile and 2-methyl-2-butenitrile (74%/18%) via the dermal route at 250, 325, 400 or 700 mg/kg-bw under occluded conditions for 24 hours and observed for 14 days following dosing. Mortality occurred at  $\geq$  325 mg/kg-bw. All deaths occurred within one day of dosing.

**LD<sub>50</sub> = 482 mg/kg-bw**

***2-Pentenenitrile (CASRN 13284-42-9)***

New Zealand White rabbits (2/dose) were administered CASRN 13284-42-9 at 63 or 125 mg/kg-bw via the dermal route under unspecified occlusive conditions for 24 hours followed by a 14-day observation period. Mortality was 100% at 125 mg/kg-bw. This study is a TSCATS submission (OTS0537162).

**LD<sub>50</sub> > 63 mg/kg-bw < 125 mg/kg-bw**

***cis-2-Pentenenitrile (CASRN 25899-50-7)***

Male albino rabbits (1/dose) were administered CASRN 25899-50-7 (purity 67.7 or 37.4%) via the dermal route at 60, 90, 130, 200, 300, 450, 670, 1500, 2500 or 4000 mg/kg-bw under occluded conditions for 24 hours, and observed for 14 days following removal of wrappings. Mortality occurred at  $\geq 300$  mg/kg-bw.

**Approximate Lethal Dose = 300 mg/kg-bw**

***Repeated-Dose Toxicity***

***cis-2-Pentenenitrile (CASRN 25899-50-7)***

(1) CRL:CD®(SD)IGS BR rats (10 or 20/sex/group) were administered CASRN 25899-50-7 by gavage at 0, 10, 30 or 75 mg/kg-bw/day for 28 (males) or 29 (females) days with or without a 2-month recovery period. An initial high-dose of 100 mg/kg-bw was reduced to 75 mg/kg-bw after 8 days due to excessive mortality. Compound-related reductions in mean body weights, body weight gain, food consumption and mean food efficiency were observed in all treated animals. Reductions in hindlimb grip strength (females only) and degeneration/atrophy of nasal dorsal olfactory mucosa in male and female rats dosed with  $\geq 10$  mg/kg-bw/day were noted. Decreased red cell mass parameters accompanied by reticulocytosis were observed in high-dose females. Most clinical signs of toxicity were at least partially reversed over the 2-month recovery phase; however, nasal histopathology did not demonstrate reversal. Neurobehavioral signs including head tilt/bob/shake, hyperactivity, hyperreactivity, abnormal gait and/or circling were noted mainly in rats dosed at an initial 100 mg/kg-bw/day or soon after the dose was reduced to 75 mg/kg-bw/day. However, none of these signs were noted during FOB and MA tests performed near the end of the dosing period. Males in the high-dose group as well as females dosed at  $\geq 10$  mg/kg-bw/day exhibited reductions in forelimb and hindlimb grip strength. At the end of the recovery phase, the reduction in hindlimb grip strength was still evident in high-dose females, although partial recovery was noted. The effects were, however, reversible at nonlethal doses.

**LOAEL = 10 mg/kg-bw/day** (based on decreased bodyweight, atrophy of nasal dorsal olfactory mucosa, reduction in forelimb and hindlimb grip strength in females)

**NOAEL = Not established**

(2) CRL:CD®BR rats (15/sex/dose) were exposed via nose-only inhalation to CASRN 25899-50-7 at concentrations of 0, 3.0, 30, 100 or 300 ppm (~ 0.01, 0.10, 0.34 and 1.0 mg/L) for 6 hours/day 5 days/week for 4 weeks (20 exposures in total). Five rats/sex/concentration were evaluated for systemic toxicity and two replicates of five rats/concentration were designated for neurobehavioral evaluation (functional observation battery [FOB] and motor activity [MA]) and neuropathology. Clinical observations were similar to controls in exposed rats. Decreased body weight and body weight gain were observed in males exposed to 30, 100 and 300 ppm, accompanied by decreased food consumption and efficiency. Sorbitol dehydrogenase activity was decreased in males and females and females exhibited decreased aspartate aminotransferase activity. Females at 300 ppm exhibited increased absolute and relative liver weights and increased relative liver weight at 100 ppm; however, microscopic changes were not observed. At  $\geq 30$  ppm, males and females exhibited microscopic evidence of primary olfactory epithelial degeneration with secondary necrotic exudate, regeneration/metaplasia and vacuolation of the olfactory nerve bundles. There were no compound-related effects on FOB and MA tests at any exposure concentration in either males or female rats. No compound-related gross or

microscopic changes in nervous tissue were observed at any concentration level.  
**LOAEL ~ 0.10 mg/L** (based on decreased male body weights, changes in sorbitol dehydrogenase activity and microscopic nasal lesions)  
**NOAEL ~ 0.01 mg/L**

### ***Reproductive/Developmental Toxicity***

No data were submitted for these endpoints.

### ***Genetic Toxicity – Gene Mutation***

#### ***In vitro***

#### ***2-Methyl-3-butenitrile (CASRN 16529-56-9)***

*Salmonella typhimurium* strains TA97, TA98, TA100, TA1535 and TA1537 were exposed to CASRN 16529-56-9 in two trials at concentrations up to 6667 µg/plate, with and without Aroclor-induced rat and/or hamster liver S9. Appropriate positive control and solvent control tests were conducted concurrently. Cytotoxicity was observed at 6666 µg/plate in the presence of S9 activation and at 3333 µg/plate in the absence of activation. The affected strains were not specified. CASRN 16529-56-9 was equivocal in strain TA97 with and without exogenous activation, but was not mutagenic in the other strains tested at any concentration, with or without S9 activation. The National Toxicology Program (NTP) concluded that 2-methyl-CASRN 4635-87-4 was not mutagenic.

**CASRN 16529-56-9 was not mutagenic in this assay.**

(2) In an additional NTP study, *Salmonella typhimurium* strains TA97, TA98, TA100, TA1535 and TA1537 were exposed to CASRN 16529-56-9 at concentrations up to 10,000 µg/plate, with and without Aroclor-induced rat and/or hamster liver S9. Appropriate positive and solvent control tests were conducted concurrently. Cytotoxicity was observed at 6666 µg/plate without metabolic activation and at 10,000 µg/plate with and without activation. In two trials, 2-methyl-CASRN 4635-87-4 was weakly positive and equivocal, respectively, without metabolic activation.

**CASRN 16529-56-9 was weakly mutagenic in this assay.**

#### ***2-Pentenenitrile (CASRN 13284-42-9)***

(1) *Salmonella typhimurium* strains TA97, TA98, TA100, TA1535 and TA1537 were exposed to CASRN 13284-42-9 at concentrations up to 6667 µg/plate, with and without Aroclor-induced rat and/or hamster liver S9. Appropriate positive control and solvent control tests were conducted concurrently, giving expected results. Cytotoxicity was observed at 3333 µg/plate in the presence of S9 activation.

**CASRN 13284-42-9 was not mutagenic with or without activation in this assay.**

(2) *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA97 were exposed to CASRN 13284-42-9 at concentrations up to 5000 µg/plate, with and without Aroclor-induced rat liver S9. Appropriate positive control and solvent control tests were conducted concurrently, but the results were not specified. Cytotoxicity was observed at 5000 µg/plate in TA98. A weak positive trend was observed in strains TA97 and TA98 and was confirmed in TA98 without

metabolic activation; however, the criteria for a positive finding were not met. This study is a TSCATS submission (OTS0529919).

**CASRN 13284-42-9 was equivocal in this assay.**

***cis-2-Pentenenitrile (CASRN 25899-50-7)***

(1) Mouse lymphoma cells (L5178Y) were exposed to CASRN 25899-50-7 at 0.1 – 1.0 /  $\mu\text{g mL}$  without Aroclor-induced rat liver S9 activation or 0.0040 – 0.04 /  $\mu\text{g mL}$  with S9 activation. Cytotoxicity was reported at 1.0  $\mu\text{g /mL}$  without activation and at 0.5  $\mu\text{g /mL}$  with activation. Both nonactivated and activated cultures produced increases in mutant frequency up to 6.3 and 4.2 times greater, respectively, than the mutant frequency of the solvent controls.

**CASRN 25899-50-7 was mutagenic in this assay.**

(2) *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 were exposed to CASRN 25899-50-7, at concentrations up to 10,000  $\mu\text{g/plate}$ , with and without Aroclor-induced rat liver S9. Appropriate positive control and solvent control tests were conducted concurrently, but the results were not specified. Cytotoxicity was determined to be > 10,000  $\mu\text{g/plate}$  in strain TA1535. This study is a TSCATS submission (OTS0529919). **CASRN 25899-50-7 was not mutagenic in this assay.**

***3-Pentenenitrile (CASRN 4635-87-4)***

*Salmonella typhimurium* strains TA97, TA98, TA100, TA104, TA1535 and TA1537 were exposed to CASRN 4635-87-4 in two studies at concentrations up to 6667  $\mu\text{g/plate}$ , with and without Aroclor-induced rat and/or hamster liver S9-mix. Appropriate positive control and solvent control tests were conducted concurrently, giving the expected results. Cytotoxicity was observed in some strains at  $\geq 3333 \mu\text{g/plate}$  with and without S9 activation. In the initial study, strain TA97 was weakly positive in two out of four trials with hamster liver S9-mix. Equivocal, weakly positive and positive results were seen in TA1535 in the presence of metabolic activation and in TA100 and TA97 without activation in the second study. Strain TA98 showed no evidence of mutagenic effects either in the presence or absence of metabolic activation.

**CASRN 4635-87-4 was weakly positive in this assay.**

***4-Pentenenitrile (CASRN 592-51-8)***

In an NTP study conducted in 2002, *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA97 were exposed to CASRN 592-51-8 at concentrations up to 10,000  $\mu\text{g/plate}$ , with and without Aroclor-induced rat or hamster liver S9. Appropriate positive and solvent control tests were conducted concurrently, giving expected results. Cytotoxicity was seen at 10,000  $\mu\text{g/plate}$  in the presence and absence of metabolic activation.

**CASRN 592-51-8 was not mutagenic in this assay.**

***Genetic Toxicity – Chromosomal Aberrations***

***In vitro***

***cis-2-Pentenenitrile (CASRN 25899-50-7)***

Chinese hamster ovary cells were exposed to CASRN 25899-50-7 at concentrations up to 810.5  $\mu\text{g/mL}$  in the presence and absence of an exogenous S9 metabolic activation system, for 4 or 20 hours in the non-activated systems and 4 hours in the activated system. All cells were harvested

20 hours after treatment initiation. Cytotoxicity was observed in the 4-hour activated cultures at  $\geq 162.1 \mu\text{g/mL}$ . The incidence of structural aberrations in the 4- and 20-hour nonactivated test systems was comparable to that of the controls, while the 4-hour S9 activated systems exhibited statistically significant ( $p < 0.05$ ) increases in structural aberrations over controls. This study is a TSCATS submission (8EHQ-0105-15899A).

**CASRN 25899-50-7 induced chromosomal aberrations in this assay.**

### *Additional Information*

#### *Skin Irritation*

##### ***2-Methyl-3-butenitrile (CASRN 16529-56-9)***

Male albino guinea pigs (10/group) were exposed to 1 drop of 100% CASRN 16529-56-9 or 50 or 25% in 1:1 solution with acetone-dioxane on shaved, intact skin. No dermal reaction was observed 1 – 2 days following treatment.

**CASRN 16529-56-9 was not irritating to guinea pig skin in this study.**

##### ***cis-2-Pentenenitrile (CASRN 25899-50-7)***

Six female New Zealand White rabbits were exposed to 0.5 mL of 98.6% CASRN 13284-42-9 on intact, shaved skin under semi-occluded conditions for 24 hours. The contact site was washed and the test sites were evaluated according to the Draize scale at 24 and 48 hours following application of the test material.

**CASRN 25899-50-7 was not irritating to rabbit skin in this study.**

##### ***3-Pentenenitrile (CASRN 4635-87-4)***

Male albino guinea pigs (10/group) were exposed to 1 drop of 100% CASRN 4635-87-4 or 43% in a 1:1 solution in acetone-dioxane containing 13% guinea pig fat on shaved, intact skin. One animal exposed to 100% CASRN 4635-87-4 exhibited mild erythema 1 day post-exposure. Reaction for primary irritation was not observed on day 2. No dermal reactions were observed in guinea pigs administered 43% CASRN 4635-87-4 1 – 2 days following treatment.

**CASRN 4635-87-4 was not irritating to guinea pig skin in this study.**

***4-Pentenenitrile (CASRN 592-51-8)*** Male albino guinea pigs (10/group) were exposed to 1 drop of 100% CASRN 592-51-8 or 48% in a 1:1 solution in acetone-dioxane containing 13% guinea pig fat on shaved, intact skin. No dermal reactions were observed 1 – 2 days following treatment.

**CASRN 592-51-8 was not irritating to guinea pig skin in this study.**

#### *Eye Irritation*

##### ***2-Methyl-3-butenitrile (CASRN 16529-56-9)***

Undiluted CASRN 16529-56-9 was instilled into the right conjunctival sac of each of two rabbits. Twenty seconds after contact, one exposed eye was washed with tap water for 1 minute, while the other exposed eye was not washed. Observations were made with a hand slit-lamp and examinations were conducted 1 day following exposure with fluorescein stain. Transient, very mild corneal injury and conjunctival irritation were seen in the unwashed eye. The similarly

dosed, promptly washed eye exhibited temporary, mild conjunctival irritation.

**CASRN 16529-56-9 was mildly irritating to rabbit eyes in this study.**

***cis-2-Pentenenitrile (CASRN 25899-50-7)***

Female New Zealand White rabbits (2/dose) were administered CASRN 13284-42-9 by instillation of 0.1 mL into the lower conjunctival sac of the left eye. Twenty seconds after contact, the eyes of one rabbit were washed for 1 minute, while the eyes of the remaining rabbit were not washed. The eyes were examined at 1 and 4 hours, and 1, 2 and 3 days following initial exposure with illumination and magnification and scored according to Draize. No irritation was observed in the treated eye that had been washed after exposure. The treated, unwashed eye exhibited moderate conjunctival redness and blood-tinged discharge. No corneal injury was revealed with fluorescein stain and biomicroscopy.

**CASRN 25899-50-7 was moderately irritating to rabbit eyes in this study.**

***3-Pentenenitrile (CASRN 4635-87-4)***

Undiluted CASRN 4635-87-4 was instilled into the right conjunctival sac of each of two rabbits. Twenty seconds after contact, one exposed eye was washed with tap water for 1 minute, while the other exposed eye was not washed. Transient, mild corneal injury and conjunctival irritation without significant iritic change was observed.

**CASRN 4635-87-4 was mildly irritating to rabbit eyes in this study.**

***4-Pentenenitrile (CASRN 592-51-8)***

Undiluted CASRN 592-51-8 was instilled into the right conjunctival sac of each of two rabbits. Twenty seconds after contact, one exposed eye was washed with tap water for 1 minute, while the other exposed eye was not washed. Observations were made with a hand slit lamp and examinations were conducted 1 day following exposure with fluorescein stain. Mild conjunctival irritation without significant iritic or corneal change was observed.

**CASRN 592-51-8 was mildly irritating to rabbit eyes in this study.**

***Skin Sensitization***

***2-Methyl-3-butenitrile (CASRN 16529-56-9)***

Male albino guinea pigs (5/group) received nine dermal applications of 100% 2-methyl-3-butenitrile or four intradermal injections (1% solution in dimethyl phthalate) over a 3-week interval. A 2-week rest period was followed by challenge applications of 100% 2-methyl-3-butenitrile or 50% solution in 1:1 acetone-dioxane to intact and abraded skin. One guinea pig receiving 100% test material on intact skin exhibited mild erythema. No other reactions were reported.

**CASRN 16529-56-9 was not a dermal sensitizer in this study.**

***3-Pentenenitrile (CASRN 4635-87-4)***

Male albino guinea pigs (5/group) received nine dermal applications of 100% CASRN 4635-87-4 or four intradermal injections (0.85% solution in dimethyl phthalate) over a 3-week interval. A 2-week rest period was followed by challenge applications of 100% CASRN 4635-87-4 or 43% solution in 1:1 acetone-dioxane containing 13% guinea pig fat to intact and abraded skin. Five guinea pigs with intact skin and six with abraded skin exhibited mild erythema one day after

exposure to 100% CASRN 4635-87-4. At 43%, six guinea pigs with abraded skin exhibited mild erythema after exposure. All reactions were negative in intact and abraded skin after 2 days and no sensitization reactions were observed.

**CASRN 4635-87-4 was not a dermal sensitizer in this study.**

***4-Pentenenitrile (CASRN 592-51-8)***

Male albino guinea pigs (5/group) received nine topical applications of 100% CASRN 592-51-8 or four intradermal injections (0.85% solution in dimethyl phthalate) over a 3-week interval. A 2-week rest period was followed by challenge applications of 100% CASRN 592-51-8 or 48% solution in 1:1 acetone-dioxane containing 13% guinea pig fat to intact and abraded skin. Two and one guinea pigs at 100 and 48%, respectively, exhibited mild erythema in intact skin one day after administration of the challenge dose. No reactions were reported at the 2-day challenge observation for intact skin and at the 1- and 2-day observations for abraded skin.

**CASRN 592-51-8 was not a dermal sensitizer in this study.**

**Conclusion:** The acute toxicity of mononitrile category members is moderate via the oral route and moderate to high via the dermal and inhalation routes. In a 29-day oral repeated-dose toxicity study in rats, CASRN 25899-50-7 showed decreased bodyweight and atrophy of nasal dorsal olfactory mucosa at 10 mg/kg-bw/day. Female rats showed reduction in forelimb and hindlimb grip strength at this dose; the NOAEL for systemic toxicity was not established. Repeated inhalation exposure of rats for 28 days to ~ 0.1 mg/L/day CASRN 25899-50-7 showed decreased male body weights, changes in sorbitol dehydrogenase activity and microscopic nasal lesions in rats; the NOAEL for systemic toxicity was ~ 0.01 mg/L/day. No data were submitted for the reproductive/developmental toxicity endpoints. Mononitrile category members induced gene mutations in bacteria and mammalian cells *in vitro*, and induced chromosomal aberrations *in vitro*. Mononitrile category members are not irritating to rabbit or guinea pig skin; however, they do cause eye irritation in rabbits. Mononitrile category members are not skin sensitizers.

**Table 6. Summary of the Screening Information Data Set under the U.S. HPV Challenge Program – Human Health Data**

<b>Endpoints</b>	<b>SPONSORED CHEMICAL 2-Methyl-3-butenitrile (16529-56-9)</b>	<b>SPONSORED CHEMICAL 2-Pentenenitrile (13284-42-9)</b>	<b>SPONSORED CHEMICAL <i>cis</i>-2-Pentenenitrile (25899-50-7)</b>	<b>SPONSORED CHEMICAL <i>trans</i>-2-Pentenenitrile (26294-98-4)</b>	<b>SPONSORED CHEMICAL 3-Pentenenitrile (4635-87-4)</b>	<b>SPONSORED CHEMICAL <i>cis</i>-3-Pentenenitrile (16545-78-1)</b>	<b>SPONSORED CHEMICAL <i>trans</i>-3-Pentenenitrile (16529-66-1)</b>	<b>SPONSORED CHEMICAL 4-Pentenenitrile (592-51-8)</b>
<b>Acute Oral Toxicity LD<sub>50</sub> (mg/kg-bw)</b>	No Data > 125 < 250 (RA)	No Data > 125 < 250 (RA)	> <b>125</b> < <b>250</b>	No Data > 125 < 250 (RA)	No Data > 125 < 250 (RA)	No Data > 125 < 250 (RA)	No Data > 125 < 250 (RA)	No Data > 125 < 250 (RA)
<b>Acute Inhalation Toxicity LC<sub>50</sub> (mg/L)</b>	<b>~ 10</b>	<b>~ 2.4</b>	<b>~ 2.81</b>	No Data ~ 1.39 (RA)	<b>~ 1.39</b>	No Data ~ 1.39 (RA)	No Data ~ 1.39 (RA)	<b>~ 8.46</b>
<b>Acute Dermal Toxicity LD<sub>50</sub> (mg/kg-bw)</b>	<b>482</b>	<b>&gt; 63 &lt; 125</b>	No Data > 63 < 125 (RA)	No Data > 63 < 125 (RA)	<b>699</b>	No Data > 63 < 125 (RA)	No Data > 63 < 125 (RA)	<b>&gt; 200</b>
<b>Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	No Data NOAEL = Not established LOAEL = 10 (RA)	No Data NOAEL = Not established LOAEL = 10 (RA)	<b>NOAEL = Not established LOAEL = 10</b>	No Data NOAEL = Not established LOAEL = 10 (RA)	No Data NOAEL = Not established LOAEL = 10 (RA)	No Data NOAEL = Not established LOAEL = 10 (RA)	No Data NOAEL = Not established LOAEL = 10 (RA)	No Data NOAEL = Not established LOAEL = 10 (RA)

**Table 6. Summary of the Screening Information Data Set under the U.S. HPV Challenge Program – Human Health Data**

<b>Endpoints</b>	<b>SPONSORED CHEMICAL 2-Methyl-3-butenenitrile (16529-56-9)</b>	<b>SPONSORED CHEMICAL 2-Pentenenitrile (13284-42-9)</b>	<b>SPONSORED CHEMICAL <i>cis</i>-2-Pentenenitrile (25899-50-7)</b>	<b>SPONSORED CHEMICAL <i>trans</i>-2-Pentenenitrile (26294-98-4)</b>	<b>SPONSORED CHEMICAL 3-Pentenenitrile (4635-87-4)</b>	<b>SPONSORED CHEMICAL <i>cis</i>-3-Pentenenitrile (16545-78-1)</b>	<b>SPONSORED CHEMICAL <i>trans</i>-3-Pentenenitrile (16529-66-1)</b>	<b>SPONSORED CHEMICAL 4-Pentenenitrile (592-51-8)</b>
<b>Repeated-Dose Toxicity NOAEL/LOAEL Inhalation (mg/L/day)</b>	No Data NOAEL ~ 0.01 LOAEL ~ 0.10 (RA)	No Data NOAEL ~ 0.01 LOAEL ~ 0.10 (RA)	<b>(4-wk) NOAEL ~ 0.01 LOAEL ~ 0.10</b>	No Data NOAEL ~ 0.01 LOAEL ~ 0.10 (RA)	No Data NOAEL ~ 0.01 LOAEL ~ 0.10 (RA)	No Data NOAEL ~ 0.01 LOAEL ~ 0.10 (RA)	No Data NOAEL ~ 0.01 LOAEL ~ 0.10 (RA)	No Data NOAEL ~ 0.01 LOAEL ~ 0.10 (RA)
<b>Reproductive Toxicity NOAEL/LOAEL (mg/kg-day)</b>	No Data							
<b>Developmental Toxicity NOAEL/LOAEL (mg/kg-day) Maternal and Developmental Toxicity</b>	No Data							
<b>Genetic Toxicity – Gene Mutation <i>In vitro</i></b>	<b>Weakly positive</b>	<b>Equivocal</b>	<b>Positive</b>	No Data Positive (RA)	<b>Weakly positive</b>	No Data Positive (RA)	No Data Positive (RA)	<b>Negative</b>
<b>Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i></b>	No Data Positive (RA)	No Data Positive (RA)	<b>Positive</b>	No Data Positive (RA)	No Data Positive (RA)	No Data Positive (RA)	No Data Positive (RA)	No Data Positive (RA)

**Table 6. Summary of the Screening Information Data Set under the U.S. HPV Challenge Program – Human Health Data**

<b>Endpoint</b>	<b>SPONSORED CHEMICAL 2-Methyl-3-butenenitrile (16529-56-9)</b>	<b>SPONSORED CHEMICAL 2-Pentenenitrile (13284-42-9)</b>	<b>SPONSORED CHEMICAL <i>cis</i>-2-Pentenenitrile (25899-50-7)</b>	<b>SPONSORED CHEMICAL <i>trans</i>-2-Pentenenitrile (26294-98-4)</b>	<b>SPONSORED CHEMICAL 3-Pentenenitrile (4635-87-4)</b>	<b>SPONSORED CHEMICAL <i>cis</i>-3-Pentenenitrile (16545-78-1)</b>	<b>SPONSORED CHEMICAL <i>trans</i>-3-Pentenenitrile (16529-66-1)</b>	<b>SPONSORED CHEMICAL 4-Pentenenitrile (592-51-8)</b>
<b>Additional Information</b>								
<b>Skin Irritation</b>	<b>Not irritating</b>	—	<b>Not irritating</b>	—	<b>Not irritating</b>	—	—	<b>Not irritating</b>
<b>Eye Irritation</b>	<b>Mildly irritating</b>	—	<b>Moderately irritating</b>	—	<b>Mildly irritating</b>	—	—	<b>Mildly irritating</b>
<b>Skin Sensitization</b>	<b>Negative</b>	—	—	—	<b>Negative</b>	—	—	<b>Negative</b>

Measured data in bold text; (RA) = Read Across; — Endpoint was not addressed for this chemical

#### **4. Hazard to the Environment**

Acute aquatic toxicity data submitted for CASRNs 16529-56-9, 13284-42-9, and 4635-87-4 were not included in this hazard characterization. EPA considers the data inadequate because nominal concentrations were used for volatile chemicals that require measured concentrations and closed test systems. A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 7. 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-Butenenitrile (CASRN 109-75-1, supporting chemical)***

Fathead minnows (*Pimephales promelas*) were exposed to the test substance (CASRN 109-75-1) at average measured concentrations of 0, 73.8, 105, 166, 240 and 350 mg/L under flow-through conditions for 96 hours. Temperature, dissolved oxygen, total hardness, total alkalinity and pH were monitored. Mortality occurred at  $\geq 173$  mg/L.

**96-h LC<sub>50</sub> = 182 mg/L**

###### ***Acrylonitrile (CASRN 107-13-1, supporting chemical)***

(1) Fathead minnows (*Pimephales promelas*) were exposed to the test substance (CASRN 107-13-1) at unspecified concentrations under static conditions in hard and soft water. In all test concentrations, analyses were made for DO, pH, alkalinity, acidity, and versenate hardness, both initially and after fish mortality or at the end of the test periods.

**96-h LC<sub>50</sub> = 14.3 – 18.1 mg/L**

(2) Bluegill sunfish (*Lepomis macrochirus*) were exposed to the test substance (CASRN 107-13-1) at a minimum of four test concentrations (unspecified) under flow-through conditions for 96 hours. The test solutions were measured. Volatilization was minimized.

**96-h LC<sub>50</sub> = 9.3 mg/L**

##### ***Acute Toxicity to Aquatic Invertebrates***

###### ***Acrylonitrile (CASRN. 107-13-1, supporting chemical)***

(1) *Daphnia magna* were exposed to the test substance (CASRN 107-13-1) under static-renewal conditions for 48 hours with 24-hour renewal intervals. The test was conducted in a closed system.

**48-h LC<sub>50</sub> = 7.6 mg/L**

(2) *Daphnia magna* were exposed to the test substance (CASRN 107-13-1) under static-renewal conditions for 48 hours with 24-hour renewal intervals.

**48-h LC<sub>50</sub> = 8.7 mg/L**

##### ***Toxicity to Aquatic Plants***

No adequate data were submitted for this endpoint.

### ***Chronic Toxicity to Fish***

#### ***Acrylonitrile (CASRN 107-13-1, supporting chemical)***

Fathead minnows (*Pimephales promelas*), bluegills (*Lepomis macrochirus*) and guppies (*Lebistes reticulatus*) were exposed to the test substance (CASRN 107-13-1) under flow-through conditions for up to 30 days. Thirty-day median tolerance limits (TLM) ranged from 2.4 to 3.0 mg/L.

**30-d ChV = 2.6 mg/L**

### ***Chronic Toxicity to Invertebrates***

#### ***Acrylonitrile (CASRN 107-13-1, supporting chemical)***

*Daphnia magna* were exposed to the test substance (CASRN 107-13-1) under static conditions with 24-hour renewal for 48 hours to 21 days.

**21-d ChV (reproduction) = 0.71 mg/L**

**Conclusion:** The 96-hr LC<sub>50</sub> value for the supporting chemical, CASRN 109-75-1, to fish, is 182 mg/L. The 96-hr LC<sub>50</sub> value for the supporting chemical, CASRN 107-13-1, to fish, is 9.3 - 18.1 mg/L and the 48-hr EC/LC<sub>50</sub> value to aquatic invertebrates is 7.6-8.7 mg/L. The 30-day chronic toxicity value of the supporting chemical, CASRN 107-13-1, to fish, is 2.6 mg/L and the 21-day chronic value for aquatic invertebrates is 0.71 mg/L.

**Table 7. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Aquatic Toxicity Data**

Endpoints	SPONSORED CHEMICALS					SUPPORTING CHEMICAL	SPONSORED CHEMICALS			SUPPORTING CHEMICAL
	4-Pentene-nitrile	2-Methyl-3-butenenitrile	3-Pentene-nitrile	<i>cis</i> -3-Pentene-nitrile	<i>trans</i> -3-Pentene-nitrile	3-Butenenitrile	2-Pentene-nitrile	<i>cis</i> -2-Pentene-nitrile	<i>trans</i> -2-Pentene-nitrile	Acrylonitrile
	(592-51-8)	(16529-56-9)	(4635-87-4)	(16545-78-1)	(16529-66-1)	(109-75-1)	(13284-42-9)	(25899-50-7)	(26294-98-4)	(107-13-1)
<b>Fish</b> <b>96-h LC<sub>50</sub> (mg/L)</b>	No Data 182 (RA)	No adequate data 182 (RA)	No adequate data 182 (RA)	No Data 182 (RA)	No Data 182 (RA)	<b>182</b>	No Data 9.3 – 18.1 (RA)	No adequate data 9.3 – 18.1 (RA)	No Data 9.3 – 18.1 (RA)	<b>9.3 – 18.1</b>
<b>Aquatic Invertebrates</b> <b>48-h EC<sub>50</sub> (mg/L)</b>	No Data 7.6 – 8.7 (RA)	No adequate data 7.6 – 8.7 (RA)	No adequate data 7.6 – 8.7 (RA)	No Data 7.6 – 8.7 (RA)	No Data 7.6 – 8.7 (RA)	–	No Data 7.6 – 8.7 (RA)	No adequate data 7.6 – 8.7 (RA)	No Data 7.6 – 8.7 (RA)	<b>7.6 – 8.7</b>
<b>Aquatic Plants</b> <b>72-h EC<sub>50</sub> (mg/L)</b>	No Data	No Data	No Data	No Data	No Data	–	No Data	No adequate data	No Data	No Data
<b>Chronic Toxicity to Fish</b> <b>30-day ChV (mg/L)</b>	No Data 2.6 (RA)	No Data 2.6 (RA)	No Data 2.6 (RA)	No Data 2.6 (RA)	No Data 2.6 (RA)	–	No Data 2.6 (RA)	No Data 2.6 (RA)	No Data 2.6 (RA)	<b>2.6</b>
<b>Chronic Toxicity to Invertebrates</b> <b>21-day ChV (mg/L)</b>	No Data 0.71 (RA)	No Data 0.71 (RA)	No Data 0.71 (RA)	No Data 0.71 (RA)	No Data 0.71 (RA)	–	No Data 0.71 (RA)	No Data 0.71 (RA)	No Data 0.71 (RA)	<b>0.71</b>

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