Initial Risk-Based Prioritization of High Production Volume (HPV) Chemicals

Alkyl Nitriles Category

Sponsored Chemicals

Propionitrile (CASRN 107-12-0)
(CA Index Name: Propanenitrile)

Butyronitrile (CASRN 109-74-0)
(CA Index Name: Butanenitrile)

Isobutyronitrile (CASRN 78-82-0)
(CA Index Name: Propanenitrile, 2-methyl-)

Prioritization Decision: Low Priority.

- Information suggests a high potential risk to workers from these chemicals, but this would be mitigated by adherence to existing NIOSH recommendations, including the Recommended Exposure Limit (REL) for CASRN 78-82-0, the International Chemical Safety Card for CASRN 107-12-0, and the Criteria Document concerning Occupational Exposure to Nitriles, Pub. #78-212, 10978.
- **No follow-up action is suggested at this time.**

Screening-level prioritizations are interim evaluations that do not constitute either final Agency determinations as to risk or final determinations as to whether sufficient data are available to characterize risk. They are based predominantly on screening-level hazard, exposure, and risk characterizations prepared by EPA using data submitted to the Agency under the HPV Challenge Program[1] and the 2006 Inventory Update Reporting (IUR)[2], and data publicly available through other selected sources. These screening-level characterizations do not constitute full risk assessments. They are intended only to support initial decisions to determine the relative priority for further assessment or risk management activities concerning HPV chemicals, and to identify data needs for individual chemicals or chemical categories. The methodology used in preparing these characterizations and prioritization decisions is available on the EPA website.[3]

[1] US EPA, HPV Challenge Program information: http://www.epa.gov/hpv/.
[2] US EPA, IUR information: http://www.epa.gov/oppt/iur/index.htm.
[3] US EPA, Methodology for Risk-Based Prioritization Under ChAMP: http://www.epa.gov/champ/pubs/rbp/method.pdf.

Screening-Level Characterization Summary

Risk Characterization

Potential Risk to Aquatic Organisms from Environmental Releases: *LOW*. The low acute toxicity to all aquatic organisms and the low potential for exposure to the category members suggests a low potential risk to fish, aquatic invertebrates, and aquatic plants from these chemicals.

Potential Risk to the General Population from Environmental Releases, Consumers, and Children: *LOW*. Although the human health hazard is high, the low exposure potential suggests a low potential risk to the general population from environmental releases, and to consumers and children.

Potential Risk to Workers: *HIGH*. The high health hazard and high relative ranking for worker exposure to all category members suggests a high potential risk to workers.

Production Volume, Use, and Release Information

The three chemicals in the alkyl nitriles category had aggregated production and import volumes in the United States between 3 million and 30 million pounds. Non-confidential information in the IUR indicates that the industrial processing and uses of the chemicals in the alkyl nitriles category include intermediates in the manufacturing of other basic organic chemicals. IUR submissions for all three chemicals do not include commercial and consumer uses. Information from the HSDB indicates that CASRN 107-12-0 is used as a chemical intermediate to manufacture di-n-propylamine and cyanoacetates, as solvent in petroleum refining, as raw material for drug manufacture, and as dielectric fluid. Information from the HSDB for CASRN 109-74-0 indicates that the chemical is used as basic material in chemical and pharmaceutical intermediates and products, and poultry medicines. Pharmaceutical and medical products are not TSCA uses and are not characterized in this report. CASRN 78-82-0 is used as an intermediate for insecticides, and as a catalyst in the polymerization of ethylene, in organic synthesis.[4] Although the HSDB reported gasoline additive uses for 78-82-0, this was not confirmed by EPA.

The HPV submission for the alkyl nitriles category states that all three chemicals are primarily used as intermediates that are chemically converted to other chemicals.[5]

No information is available on releases of the category members to the environment.

[4] HSDB, 2008. Hazardous Substances Data Bank. Accessed, 8/11/08, Alkyl Nitrile Category. http://toxnet.nlm.nih.gov/ .

[5] Eastman Chemical and Solutia, 2004. Alkyl Nitriles Test Plan and Category Justification. Accessed, 8/8/08. http://www.epa.gov/chemrtk/pubs/summaries/alkyntrl/c14860tp.pdf

Hazard Characterization Summary

The members of this category are liquids with high water solubility and high vapor pressure and are expected to have high mobility in soil. The rate of biodegradation for CASRN 78-82-0 is considered rapid based on the results of a ready biodegradation test and estimated to be moderate for CASRNs 107-12-0 and 109-74-0. The rate of volatilization of the category members from water and moist soil is considered moderate given their estimated Henry's Law constants. Bioconcentration for the category members is expected to be low. The rate of hydrolysis is considered negligible under environmental conditions. The category members are expected to have low persistence (P1) and low bioaccumulation potential (B1).

The evaluation of available data indicates that the potential acute hazard to fish, aquatic invertebrates, and aquatic plants is low.

Acute toxicity of the category members is high via oral and dermal routes and moderate via inhalation. Results of mechanistic studies indicate that CASRNs 107-12-0 and 109-74-0 are activated by the liver to release cyanide, which is responsible for acute effects that are associated with cyanide toxicity. Systemic toxicity is high following repeated oral and inhalation exposures in rats in the repeated-dose toxicity studies with CASRN 107-12-0. No effects were seen on reproductive parameters in male and female fertility studies via inhalation or on reproductive organs in the repeated-dose toxicity studies with CASRN 107-12-0. Prenatal developmental toxicity study in rats with CASRN 107-12-0 via oral route showed high maternal and developmental toxicity. However, prenatal developmental studies in rats with CASRNs 109-74-0 and 78-82-0 via inhalation showed moderate developmental toxicity. The category members did not induce gene mutation or chromosomal aberrations. CASRN 107-12-0 was irritating to rabbit eyes and slightly irritating to rabbit skin.

No data gaps were identified under the HPV Challenge Program.

Exposure Characterization Summary

EPA identifies a low potential that the general population and the environment might be exposed to the category members through environmental releases based on the limited releases (these chemicals are used primarily intermediates) and environmental fate.

EPA identifies a low potential for exposure to consumers and children because the category members are not used in consumer products or products intended for use by children.

EPA identifies high relative rankings for potential worker exposures for the category chemicals based primarily on the high vapor pressures of these chemicals.

Additional Considerations For Prioritization Decision

Regulatory and Related Information Summary

- The category chemicals are listed on the TSCA Inventory.

- EPA regulates CASRN 107-12-0 on the Equipment Leaks list under Section 111 of the Clean Air Act and CASRN 109-74-0 on the same list for volatility reasons.
- EPA regulates CASRNs 107-12-0 and 78-82-0 as Extremely Hazardous Substances based on toxicity under Section 112(r) of the Clean Air Act.
- EPA regulates CASRN 107-12-0 in RCRA Appendix VIII & P Waste based on acute toxicity.
- CASRN 107-12-0 is included in CERCLA.
- EPA regulates CASRNs 107-12-0 and 78-82-0 in SARA 302A as Extremely Hazardous Substances.
- CASRN 78-82-0 is included in TRI reporting as a component of "cyanide compounds."
- There is a NIOSH International Chemical Safety Card for CASRN 107-12-0.
- All 3 category members are addressed in NIOSH Criteria Document, Occupational Exposure to Nitriles, Pub. #78-212, 10978.
- There is a NIOSH Recommended Exposure Limit (REL) of 8 ppm TWA for CASRN 78-82-0.

Assumptions and Uncertainties

- EPA has no information on releases of these chemicals, other than CASRN 78-82-0 being included as a component of cyanide compounds for TRI reporting. EPA assumes potential exposures based on reported uses. In this case, these chemicals have been identified as chemical intermediates, which is an indication of low releases. The lack of environmental release data for a chemical is a source of uncertainty in the potential that the general population and the environment might be exposed to that chemical. Worker exposure will not exceed the Recommended Exposure Limit (REL) in workplaces.

Appendix A: Screening-Level Hazard Characterization

CHEMICAL CATEGORY NAME
Alkyl Nitriles

SPONSORED CHEMICALS

Propionitrile (CASRN 107-12-0)
[CA Index Name: Propanenitrile]

Butyronitrile (CASRN 109-74-0)
[CA Index Name: Butanenitrile]

Isobutyronitrile (CASRN 78-82-0)
[CA Index Name: Propanenitrile, 2-methyl-]

Introduction

The sponsors, Eastman Chemical Company and Solutia Inc., submitted a Test Plan and Robust Summaries to EPA for the Alkyl Nitriles Category on November 17, 2003. EPA posted the submission on the ChemRTK HPV Challenge website on December 19, 2003 (http://www.epa.gov/chemrtk/pubs/summaries/alkyntrl/c14860tc.htm). EPA comments on the original submission were posted to the website on May 5, 2004. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on June 12, 2004, which were posted to the ChemRTK website on September 1, 2004. The Alkyl Nitriles Category consists of the following chemicals:

Propionitrile (CASRN 107-12-0)
[CA Index Name: Propanenitrile]

Butyronitrile (CASRN 109-74-0)
[CA Index Name: Butanenitrile]

Isobutyronitrile (CASRN 78-82-0)
[CA Index Name: Propanenitrile, 2-methyl-]

Category Justification

All three category members have closely related molecular and generic chemical structure and the same functionality. The category members differ in having either two or three carbons in the alkyl chain, and in the case of the butyronitrile and isobutyronitrile members, the only difference is in their alky chain branching. The generic structure of the category members is depicted as:

RC≡N, where R = CH3CH2-, CH3CH2CH2- or (CH3)2CH-

The nitrile functional group of these chemicals is responsible for their chemical behavior. A putative metabolite of all three materials is cyanide. The acute and repeated-dose toxicity for the category members is similar to that of cyanide. In addition, the relatively short aliphatic hydrocarbon side chains and lack of reactive functional groups result in very similar physicochemical characteristics and environmental fate properties among the three chemicals. Data submitted for the ecotoxicity and human health endpoints show similarities among the three compounds with respect to toxic effects and effect levels. The sponsor included data showing that the mode of action for the mammalian toxicities of the alkyl nitriles is cyanide intoxication. EPA agrees with the sponsor's category justification and further accepts this category for prioritization in the ChAMP.

1. Physical-Chemical Properties and Environmental Fate

The physical-chemical properties of compounds in the alkyl nitriles category are summarized in Table 1a and their environmental fate properties are given in Table 1b. The structures of the compounds are provided in Table 4 at the end of Appendix A.

Physical-Chemical Properties Characterization

The alkyl nitriles are liquids with high water solubility and high vapor pressure.

Table 1a. Physical-Chemical Properties of Alkyl Nitriles Category[1]

Property	Propionitrile	Butyronitrile	Isobutyronitrile
CASRN	107-12-0	109-74-0	78-82-0
Molecular Weight	55.08	69.11	69.11
Physical State	Liquid	Liquid	Liquid
Melting Point	-92.8°C (measured)	-112°C (measured)	-71.5°C (measured)
Boiling Point	97°C (measured)	117.5°C (measured)	103.8°C (measured)
Vapor Pressure	39 mm Hg at 20°C (measured); 40 mm Hg at 22°C (measured)	10 mm Hg at 15°C (measured); 20 mm Hg at 25°C (extrapolated); 40 mm Hg at 38°C (measured)	47 mm Hg at 23°C (measured)
Water Solubility	93,380 mg/L at 25°C (measured); 119,000 mg/L at 40°C (measured)	33,000 mg/L at 25°C (measured)	39,000 mg/L at 25°C (measured)
Dissociation Constant (pK_a)	Not applicable	Not applicable	Not applicable
Henry's Law Constant	4.06×10^{-5} atm-m^3/mole (estimated)[2]	5.38×10^{-5} atm-m^3/mole (estimated)[2]	5.38×10^{-5} atm-m^3/mole (estimated)[2]
Log K_{ow}	0.16 (measured)	0.53 (measured)	0.46 (measured)

[1]Eastman Chemical Company and Solutia Inc. July 1, 2004. Revised Robust Summary and Test Plan for Alkyl Nitriles Category (posted September 1, 2004). http://www.epa.gov/oppt/chemrtk/pubs/summaries/alkyntrl/c14860tc.htm.
[2]USEPA. 2008. Estimation Programs Interface Suite™ (version 3.20). United States Environmental Protection Agency, Washington, DC, USA Available online at: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.

Environmental Fate Characterization

The alkyl nitriles are expected to have high mobility in soil. The rate of biodegradation for isobutyronitrile is rapid based on the results of a ready biodegradation test and estimated to be moderate for propanenitrile and butanenitrile. The rate of volatilization of the alkyl nitriles from water and moist soil is moderate given their estimated Henry's Law constants. Biococentration for the alkyl nitriles is expected to be low. The rate of hydrolysis is considered negligible under environmental conditions. The alkyl nitriles are expected to have low persistence (P1) and low bioaccumulation potential (B1).

Table 1b. Environmental Fate Characteristics of Alkyl Nitriles Category[1]			
Property	**Propionitrile**	**Butyronitrile**	**Isobutyronitrile**
CASRN	107-12-0	109-74-0	78-82-0
Photodegradation Half-life	55.2 days (estimated; assumes 12-hour day and 1.5×10^6 hydroxyl radicals/cm^3)	21.5 days (estimated; assumes 12-hour day and 1.5×10^6 hydroxyl radicals/cm^3)	15.2 days estimated; assumes 12-hour day and 1.5×10^6 hydroxyl radicals/cm^3)
Hydrolysis Half-life	Stable	Stable	Stable
Biodegradation	Half-life = weeks (estimated)[2]	Half-life = weeks (estimated)[2]	88.2–100% in 14 days (measured)[3] Readily biodegradable
Bioconcentration	BCF = 3.2 (estimated)[2]	BCF = 3.2 (estimated)[2]	BCF = 3.2 (estimated)[2]
Log K_{oc}	0.92 (estimated)	1.18 (estimated)	1.1 (estimated)[2]
Fugacity (Level III Model)[2]	Air = 14.4% Water = 48.7% Soil = 36.9% Sediment = 0.0821%	Air = 15% Water = 47.9% Soil = 37% Sediment = 0.0821%	Air = 17.8% Water = 47.3% Soil = 34.7% Sediment = 0.0809%
Persistence[4]	P1 (low)	P1 (low)	P1 (low)
Bioaccumulation[4]	B1 (low)	B1 (low)	B1 (low)

[1]Eastman Chemical Company and Solutia Inc. July 1, 2004. Revised Robust Summary and Test Plan for Alkyl Nitriles Category (posted September 1, 2004). http://www.epa.gov/oppt/chemrtk/pubs/summaries/alkyntrl/c14860tc.htm.
[2]USEPA. 2008. Estimation Programs Interface Suite™ (version 3.20). United States Environmental Protection Agency, Washington, DC, USA Available online at: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.
[3]National Institute of Technology and Evaluation. 2002. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. Accessed August 29, 2008. http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html.
[4]Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

Conclusion: The alkyl nitriles are liquids with high water solubility and high vapor pressure. They are expected to have high mobility in soil. Volatilization of the alkyl nitriles is considered moderate based upon their Henry's Law constants. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered negligible. The alkyl nitriles are expected to have low persistence (P1) and low bioaccumulation potential (B1).

2. Environmental Effects – Aquatic Toxicity

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

Acute Toxicity to Fish

Propionitrile (CASRN 107-12-0)

(1) Fathead minnows (*Pimephales promelas*) were exposed to measured concentrations of 0, 375, 611, 887, 1100 and 2188 mg/L under flow–through conditions for 96 hours. One fish exposed to 1100 mg/L and all fish exposed to 2188 mg/L died by 24 hours.

96-h LC_{50} = 1520 mg/L

(2) Bluegill sunfish (*Lepomis macrochirus*) were exposed to nominal concentrations of 0, 10, 18, 32, 56 and 100 mg/L under static conditions for 96 hours. Mortality was 10% in the 10 and 18 mg/L groups. The mortality rate for fish exposed to 32 mg/L was 20% at 24 hours, 20% at 48 hours, 40% at 72 hours, and 50% at 96 hours. The mortality rate for fish exposed to 56 mg/L was 0% at 24 hours, 40% at 48 and 72 hours, and 50% at 96 hours. The mortality rate for fish exposed to 100 mg/L was 50% at 24 hours, and 90% at 48, 72 and 96 hours.
96-h LC_{50} = 41 mg/L

(3) Rainbow trout (*Salmo gairdneri*) were exposed to nominal concentrations of 0, 100, 180, 320, 560 and 1000 mg/L under static conditions for 96 hours. None of the fish exposed to 100 or 180 mg/L died. The mortality rate for fish exposed to 320 mg/L was 10% at 24 hours, 20% at 48 hours, 30% at 72 hours, and 40% at 96 hours. The mortality for fish exposed to 560 or 1000 mg/L was 100% by 24 hours.
96-h LC_{50} = 340 mg/L

Butyronitrile (CASRN 109-74-0)
Fathead minnow (*Pimephales promelas*) were exposed to mean measured concentrations of 107 mg/L under static conditions for 96 hours. No mortality occurred and all fish exhibited normal behavior and appearance.
96-h LC_{50} > 107 mg/L

Isobutyronitrile (CASRN78-82-0)
Fathead minnow (*Pimephales promelas*) were exposed to mean measured concentrations of 102.1 mg/L under static conditions for 96 hours. No mortality occurred and all fish exhibited normal behavior and appearance.
96-h LC_{50} > 102.1 mg/L

Acute Toxicity to Aquatic Invertebrates

Propionitrile (CASRN 107-12-0)
Water fleas (*Daphnia magna*) were exposed to a measured concentration of propionitrile at 0, 100, 180, 320, 560 and 1000 mg/L under static conditions for 48 hours. None of the controls or daphnids exposed to 100 mg/L died during the study. Immobilization was observed at 180 mg/L between 24 and 48 hours in one daphnid. Immobilization of daphnids exposed to 180 mg/L was 5% at 24 hours and 20% at 48 hours and exposed to 320 mg/L was 50% at 24 hours and 75% at 48 hours. All daphnids exposed to 560 or 1000 mg/L exhibited immobilization within 24 hours.
48-h EC_{50} > 250 mg/L

Butyronitrile (CASRN 109-74-0)
Water fleas (*Daphnia magna*) were exposed to a mean measured concentration of 110 mg/L under static conditions for 48 hours. All daphnids, but one (immobilization), exposed to the test-article exhibited behavior comparable to controls.
48 h EC_{50} > 110 mg/L

Isobutyronitrile (CASRN 78-82-0)
Water fleas (*Daphnia magna*) were exposed to mean measured concentration of 94.3 mg/L under static conditions for 48 hours. All daphnids exposed to test-article exhibited behavior comparable to controls.
48 h EC_{50} > 94.3 mg/L

Toxicity to Aquatic Plants

Propionitrile (CASRN 107-12-0)
No test data were submitted for propionitrile. A 96-hour ECOSAR estimated EC_{50} value for green algae was provided.
96-h EC_{50} = 789 mg/L

Butyronitrile (CASRN 109-74-0)
Green algae (*Pseudokirchneriella subcapitata*) were exposed to mean measured concentration 133.4 mg/L under static conditions for 72 hours. Algae exposed to test material exhibited normal growth with respect to control.
EC_{50} > 133.4 mg/L

Isobutyronitrile (CASRN 78-82-0)
Green algae (*Pseudokirchneriella subcapitata*) were exposed to mean measured concentration 87.8 mg/L under static conditions for 72 hours. Algae exposed to test material exhibited normal growth with respect to control.
EC_{50} > 87.8 mg/L

Conclusion: The evaluation of available aquatic toxicity data for fish, aquatic invertebrates and aquatic plants indicates that the potential acute hazard of the alkyl nitriles category members to aquatic organisms is low.

Table 2. Summary of Environmental Effects – Aquatic Toxicity Data			
Endpoints	**Propionitrile (107-12-0)**	**Butyronitrile (109-74-0)**	**Isobutyronitrile (78-82-0)**
Fish 96-h LC_{50} (mg/L)	**41 – 1520 (m)**	**> 107 (m)**	**> 102.1 (m)**
Aquatic Invertebrates 48-h EC_{50} (mg/L)	**250 (m)**	**> 110 (m)**	**> 94.3 (m)**
Aquatic Plants 72-h EC_{50} (mg/L) (growth and biomass)	No Data > 133.4 (RA) 789 (e)	**> 133.4 (m)**	**> 87.8 (m)**

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

3. Human Health Effects

A summary of health effects data submitted for SIDS endpoints is provided in Table 3. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Oral Toxicity

Propionitrile (CASRN 107-12-0)
(1) Sprague-Dawley rats (5/sex/dose) were administered propionitrile via gavage at 25.1, 31.6, 39.8, 50.1, 63.1 or 79.4 mg/kg-bw and observed for 14 days.
LD_{50} = 40 mg/kg-bw

(2) Sprague-Dawley rats (5/sex/dose) were administered propionitrile via gavage at 50.1, 63.1, 79.4, 100, 126, 158 mg/kg-bw (males) and 158, 200, 251, 316 mg/kg-bw (females).
LD_{50} (male) = 75 mg/kg-bw
LD_{50} (female) = 270 mg/kg-bw

Butyronitrile (CASRN 109-74-0)

(1) Rats (21, strain, sex distribution not reported) were administered butyronitrile via gavage at doses ranging from 25 – 3200 mg/kg-bw and observed for 14 days. All animals receiving 100 mg/kg-bw and above died within 1 day of exposure.
LD_{50} = 50 – 100 mg/kg-bw

(2) Carworth-Winstar rats (5 males/dose) were administered butyronitrile via gavage and observed for 14 days. Doses (not reported) were arranged in a logarithmic series differing by a factor of 2. Other study details were not provided.
LD_{50} = 111 mg/kg-bw

Isobutyronitrile (CASRN 78-82-0)
(1) Carworth-Winstar rats (5 males/dose) were administered isobutyronitrile via gavage and observed for 14 days. Doses (not reported) were arranged in a logarithmic series differing by a factor of 2. No other study details were reported.
LD_{50} = 77 mg/kg-bw

(2) Rats (20, strain and sex distribution not reported) were administered isobutyronitrile via gavage at doses ranging from 10 – 3200 mg/kg-bw and observed for 14 days. Mortality occurred within 15 minutes to 1 day following exposure.
LD_{50} = 50 mg/kg-bw

(3) Rats (5, strain and sex distribution not reported) were administered isobutyronitrile via gavage at doses ranging from 25 to 400 mg/kg-bw and observed for 14 days. Mortality occurred within 1 to 4 hours following exposure.
LD_{50} = 50 – 100 mg/kg-bw

Acute Dermal Toxicity

Propionitrile (CASRN 107-12-0)
In three separate studies, New Zealand White rabbits (5/sex/dose) were administered propionitrile (from three different manufacturers) dermally on to closely clipped intact skin at 12.5, 25, 50 or 100 mg/kg-bw under occluded conditions for 24 hours and observed for 14 days. Mortality occurred at the two high doses. Slight to very slight erythema was evident among 50% of the survivors.
LD_{50} = 40 – 90 mg/kg-bw

Butyronitrile (CASRN 109-74-0)
New Zealand White rabbits (4 males/dose) were administered butyronitrile dermally on to fur-clipped trunk of rabbits at various concentrations (not listed) under occluded conditions for 24 hours and observed for 14 days. Other study details were not reported.
LD_{50} = 398 mg/kg-bw

Isobutyronitrile (CASRN 78-82-0)
New Zealand White rabbits (4 males/dose) were administered butyronitrile dermally on to fur-clipped trunk of rabbits at various concentrations (not listed) under occluded conditions for 24 hours and observed for 14 days. Other study details were not reported.
LD_{50} = 239 mg/kg-bw

Acute Inhalation Toxicity

Propionitrile (CASRN 107-12-0)
Sprague-Dawley rats (5/sex/concentration) were exposed to propionitrile vapor at 1.58, 2.51, 3.98, 6.31, 10.0 or 15.8 mg/L for 4 hours and observed for 14 days. Deaths occurred within 2 – 24 hours following exposure at 2.51 mg/L and above.

LC_{50} = 3.3 mg/L

Butyronitrile (CASRN 109-74-0)
(1) Sprague-Dawley rats (5/sex) were exposed to butyronitrile vapor at 1147 ppm (~3.2 mg/L for males) or 1220 ppm (~ 3.4 mg/L for females) for 1 hour and observed for 14 days. All rats survived the study duration.
1-h LC_{50} > ~ 3.4 mg/L

(2) Sprague-Dawley rats (5/sex/concentration) were exposed to butyronitrile vapor at 1972, 4421, 6296 and 8261 ppm (~5.6, 12.5, 17.8, and 23.4 mg/L, respectively) for 1 hour. Mortality was extensive at the top three concentrations and occurred on day 1. At 1972 ppm, one animal died on day 1. An LC_{50} could not be calculated. LC_{10} was reported to be 5.2 mg/L.

Isobutyronitrile (CASRN 78-82-0)
(1) Sprague-Dawley rats (5/sex/concentration) were exposed to isobutyronitrile vapor at 1200 ppm (~3.4 mg/L) for 1 hour and observed for 14 days. All rats survived the study duration.
1-h LC_{50} > ~3.4 mg/L

(2) Sprague-Dawley rats (5/sex/concentration) were exposed to isobutyronitrile vapor at 1248, 1778 and 2709 ppm (~3.5, 5.0 and 7.7 mg/L, respectively). Deaths were 1/10, 5/10 and 8/10 at 1246, 1778 and 2709 ppm, respectively. An LC_{50} was not calculated. LC_{10} was reported to be approximately 3.3 mg/L.

Repeated-Dose Toxicity

Propionitrile (CASRN 107-12-0)

(1) Sprague-Dawley rats (15/sex/concentration) were exposed (whole body) to propionitrile vapor at 0, 60, 120 or 209 ppm (approximately 0.135, 0.271 and 0.472 mg/L/day, respectively) for 6 hours/day, 5 days/week for 14 weeks. Signs of toxicity seen at all exposure concentrations included labored breathing, nasal discharge, salivation, discharge from the eyes, hypoactivity and/or alopecia. The incidence of these signs increased in a dose-dependent manner. All exposed animals had significant decreases in red blood cells and hemoglobin values (significance was not reported). The total amount of urine thiocyanate concentrations increased with exposure concentration.

At 209 ppm three males died. Mean corpuscular hemoglobin concentration was decreased significantly ($p<0.05$) in males. Animals showed significantly ($p<0.01$) decreased body weights. Absolute and/or relative heart, liver, kidney and testes weights were increased in males and/or females; however, no histopathological correlation was seen. Absolute and/or relative spleen weights were increased in males and/or females and microscopic examination revealed hemosiderin deposits in 10/15 females.

At 120 ppm, ataxia (2 females), decreased body weight (males, $p<0.05$) and increased absolute and/or relative spleen weights (males) were seen. Mean corpuscular hemoglobin concentration in males was decreased significantly ($p<0.05$). Microscopic examination showed increased hemosiderin deposition in spleens of 11/15 females.

At 60 ppm, absolute and relative spleen weights were increased in males.

LOAEL ~ 0.135 mg/L/day (based on signs of toxicity, effects on hematology parameters and effects on spleen)

NOAEL = Not established

(2) Albino rats (5/sex/dose, strain not reported) were exposed to propionitrile via drinking water at 0, 2.5, 12.5 and 62.5 mg/L/day for 28 days. The calculated mean intakes of propionitrile were 0, 0.32, 1.34 and 3.72 mg/kg-bw/day, respectively. At 3.72 mg/kg-bw/day there was one death that occurred on day14; this animal had hemorrhagic lungs. Slightly decreased food consumption and significantly decreased body weight gain compared to the control group were seen in both sexes indicating a definite impairment of efficiency of food utilization. There were no differences between the two lower concentrations and the control groups for mortality, food intake and body weight gain.

LOAEL = 3.72 mg/kg-bw/day (based on mortality, decreased food consumption and decreased in body weight gain)

NOAEL = 1.34 mg/kg-bw/day

Reproductive Toxicity

Propionitrile (CASRN 107-12-0)

The sponsor conducted two fertility studies in which male rats were exposed in one study and were mated with virgin females; and a second study in which female rats were exposed and mated with virgin males. The conventional reproductive toxicity study was not conducted in which both treated sexes were mated to evaluate functional aspects of reproduction. Based on

EPA's comments, the sponsor submitted information on the evaluation of reproductive organs from the 14-week repeated-dose toxicity study. EPA considers this information and the non-conventional fertility studies, along with the available developmental toxicity study, adequate for the purposes of the HPV Challenge Program to address reproductive toxicity.

(1) Female Sprague-Dawley rats (24/concentration) were exposed (whole body) to propionitrile vapor at 0, 60, 120 or 210 ppm (approximately 0.14, 0.27 and 0.47 mg/L/day, respectively) for 6 hours/day for 21days and were randomly mated with untreated males. Females continued the exposure regime until gestation day 13 or 15. There was no mortality and no effect on maternal body weight. Animals exposed to 210 ppm exhibited signs of toxicity (arched back, lacrimation, salivation, hypoactivity, staining of facial fur and red nasal encrustation). (Hematology, clinical chemistry and urinalysis parameters were not evaluated during this study.) Alopecia was observed in a dose-dependent manner. At necropsy bilateral uterine hydrometra was seen in one animal at 210 ppm and in the left uterine horn in one animal at 120 ppm. There was no observed effect on fertility. Efficiency of mating was 32.0, 32.0, 30.7 and 25.0% (no statistical significance was provided) and pregnancy rates were 100, 95.8, 100 and 91.3% at 0, 60, 120 and 210 ppm, respectively. The numbers of live implants, resorptions, nidations, corpora lutea, pre- and post-implantation losses were not affected by treatment.
NOAEL (reproductive toxicity) ~ 0.47 mg/L/day (based on no effects at the highest dose tested)

(2) Male Sprague-Dawley rats (15/group) were exposed (whole body) to propionitrile vapor at 0, 60, 120 or 210 ppm (approximately 0.14, 0.27 and 0.47 mg/L/day, respectively) for 6 hours/day for 46 days and were randomly mated with untreated females. One-half of the males in each group were examined for gross lesions of the testes, epididymides, prostate glands and seminal vescicles. Mated females were euthanized on gestation day 13 and gross necropsies were performed and pregnancy status, nidation sites and the number of corpora lutea were determined. (Hematology, clinical chemistry and urinalysis parameters were not evaluated during this study.) During exposure body weights of animals exposed to 210 ppm remained lower than those of controls, but were similar at study termination, following a 2-week recovery period. Animals exposed to 210 ppm exhibited signs associated with cyanide toxicity (arched back, hypoactivity, labored breathing and salivation, grinding teeth, head bobbing, body tremors, involuntary movement and pawing at the cage). A few animals exposed to 120 ppm exhibited salivation and hypoactivity. Signs of toxicity generally disappeared by the morning following exposure. Alopecia was also observed. Gross necropsy revealed one animal in the 120 ppm dose group with a small right testis. Efficiency of mating was 34.4, 30.6, 29.8 and 27.1% (no statistical significance was provided) and pregnancy rates were 90.5, 97.6, 90.0 and 97.4% at 0, 60, 120 and 210 ppm, respectively. The numbers of live implants, resorptions, corpora lutea, pre- and post-implantation losses were not affected by treatment. Although the decrease in mating efficiency was dose-related, pregnancy rates were unaffected; therefore, the NOAEL was established at the high dose.
NOAEL (reproductive toxicity) ~ 0.47 mg/L/day (based on no effects at the highest dose tested)

(3) In the 14-week inhalation repeated-dose toxicity study described previously, reproductive organs were evaluated. The absolute left testes weights were decreased in males exposed to the highest concentration 209 ppm (~ 0.47 mg/L/day). Histopathological examination did not reveal any effect to correlate with this finding. There were no histopathological changes in the ovaries, testes (with epididymides), pituitary, prostate, uterus (with cervix), mammary gland or thyroid.

Developmental Toxicity

Propionitrile (CASRN 107-12-0)
Pregnant female Sprague-Dawley rats (25/dose) were administered propionitrile via gavage at 0, 20, 40 or 80 mg/kg-bw/day during gestation days 6-19. There was no treatment-related effect on survival. At the high dose, there was a reduction in mean maternal body weight gain over the entire treatment period. The mean maternal adjusted body weight (body weight gain minus the uterus and its contents) of the high-dose females was also reduced compared to controls. There was no treatment-related effect on the mean number of viable fetuses, late resorptions, total implantations or corpora lutea. At 80 mg/kg-bw/day, there was a significant (significance not provided) increase in the number of early resorptions (2.0 in treated vs. 0.7 in controls) and a corresponding increase in the number of post-implantation losses. There was no effect of treatment in fetal sex ratio. The mean fetal body weight was significantly (significance not provided) decreased (3.0 g in treated vs. 3.5 g in control) at the high dose compared to controls. Malformations of the fetuses (and litters) were 5(3), 1(1), 1(1) and 0(0) at 0, 20, 40 and 80 mg/kg-bw/day, respectively. An increase in the number of fetuses and litters with unossified 5 and/or 6 sternebrae was noted at the mid-dose (55 and 35, respectively) and high-dose (92 and 66.7, respectively) compared to controls (21 and 14, respectively). In addition, an increase in the number of fetuses and litters with sternebrae 1 and/or 2, 3 and 4 unossified was seen at the high-dose (8 in 2 treated litters vs. 1 in control).
LOAEL (maternal toxicity) = 80 mg/kg-bw/day (based on reduced body weight gain)
NOAEL (maternal toxicity) = 40 mg/kg-bw/day
LOAEL (developmental toxicity) = 40 mg/kg-bw/d (based on developmental variations–unossified sternebrae)
NOAEL (developmental toxicity) = 20 mg/kg-bw/day

Butyronitrile (CASRN 109-74-0)
Pregnant female Sprague-Dawley rats (20-23/dose) were exposed to butyronitrile vapor at 0, 50, 100, 150 or 200 ppm (~ 0.14, 0.28, 0.42 or 0.56 mg/L/day, respectively) 6 hours/day during gestation days 6 – 21. All animals survived the study duration. There was no treatment-related effect on maternal body weight gain, the mean number of implants, the incidence of non-surviving implants and resorptions. The mean number of live fetuses and sex ratios were not affected at any concentration. There was a concentration-dependent trend toward a decrease in fetal body weight with weights of fetuses significantly (statistical significance not provided) decreased at 200 ppm (5.08 g/litter in treated vs. 5.41 g/litter in control). The incidence of visceral and skeletal variations in treated fetuses was similar to controls.
NOAEL (maternal toxicity) ~ 0.56 mg/L/day (based on no effects at the highest dose tested)
LOAEL (developmental toxicity) ~ 0.56 mg/L/day (based on decreased fetal body weight)

NOAEL (developmental toxicity) ~ 0.42 mg/L/day

Isobutyronitrile (CASRN 78-82-0)
Pregnant female Sprague-Dawley rats (21/dose) were exposed to isobutyronitrile vapor at 0, 50, 100, 200 or 300 ppm (~ 0.14, 0.28, 0.56 or 0.84 mg/L/day, respectively) 6 hours/day during gestation days 6 – 21. One animal exposed to 200 ppm and 3 exposed to 300 ppm died prior to study termination. There was no effect on maternal body weight gain. The indices of non-surviving implants and embryonic resorptions (per litter) at 300 ppm (11.07 per litter for both indices) were significantly (significance not provided) higher than controls (2.02 per litter for both indices); however, the mean number of live fetuses and sex ratio were unaffected. A decrease in fetal body weights was noted at 200 ppm (females) and 300 ppm (males and females). One case of unilateral hydronephrosis was observed in one fetus from the 300 ppm group. The incidences of visceral and skeletal variations in treated fetuses were comparable to controls.
LOAEL (maternal toxicity) ~ 0.56 mg/L/day (based on mortality)
NOAEL (maternal toxicity) ~ 0.28 mg/L/day
LOAEL (developmental toxicity) ~ 0.56 mg/L/day (based on decreased fetal body weight in females)
NOAEL (developmental toxicity) ~ 0.28 mg/L/day

Genetic Toxicity – Gene Mutation

In vitro
Propionitrile (CASRN 107-12-0)
(1) In two NTP assays, *Salmonella typhimurium* strains TA 97, TA98, TA100, TA1535 were exposed to propionitrile at 0 (DMSO), 100, 333, 1000, 3333 and 10, 000 µg/plate with and without metabolic activation. Positive and negative controls were tested concurrently and provided appropriate response. No cytotoxicity or mutagenicity was observed in the presence or absence of metabolic activation.
Propionitrile was not mutagenic in these assays.

(2) In two studies, mouse lymphoma L5178Y cells were exposed to propionitrile at 2143, 2714, 3286, 3857, 4429 or 5000 µg/mL in the presence and absence of metabolic activation. All cultures exhibited mutant frequencies similar to the negative (solvent, DMSO) controls. All positive controls responded appropriately.
Propionitrile was not mutagenic in these assays.

Butyronitrile (CASRN 109-74-0)
Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and *Escherichia coli* (WP2uvrA (pkM101) were exposed to butyronitrile at 100, 333, 1000, 3333 or 5000 µg/plate in the presence and absence of metabolic activation. None of the tested concentrations were cytotoxic. No increase in mutant frequency was evident at any concentration. Positive and negative controls were tested concurrently and responded appropriately.
Butyronitrile was not mutagenic in this assay.

Isobutyronitrile (CASRN 78-82-0)
(1) *Salmonella typhimurium* strains TA98, TA100, TA1535, TA 1537 and *E. coli* (WP2uvrA (pkM101) were exposed to isobutyronitrile at 100, 333, 1000, 3333 or 5000 μg/plate in the presence and absence of metabolic activation. None of the tested concentrations were cytotoxic. No increase in mutant frequency was evident at any concentration. Positive and negative controls were tested concurrently and responded appropriately.
Isobutyronitrile was not mutagenic in this assay.

(2) In an NTP assays, *Salmonella typhimurium* strains TA 97, TA98, TA100, TA1535 were exposed to isobutyronitrile at 0 (DMSO), 100, 333, 1000, 3333 and 10, 000 μg/plate with and without metabolic activation. Positive and negative controls were tested concurrently and provided appropriate response. No cytotoxicity or mutagenicity was observed in the presence or absence of metabolic activation.
Isobutyronitrile was not mutagenic in these assays.

Genetic Toxicity – Chromosomal Aberrations

In vitro
Propionitrile (CASRN 107-12-0)
In an NTP assay, Chinese hamster ovary (CHO) cells were exposed to propionitrile at concentrations up to 4410 μg/mL with and without metabolic activation. Positive and negative controls were tested concurrently and provided appropriate response. Cytotoxic concentration was seen above 4410 μg/mL. Propionitrile did not induce chromosomal aberrations with or without metabolic activation.
Porpionitrile did not induce chromosomal aberrations in this assay.

Butyronitrile (CASRN 109-74-0)
Chinese hamster ovary (CHO) cells were exposed to butyronitrile at concentrations of 4.77, 6.81, 9.73, 13.9, 19.9, 28.4, 40.5, 57.8, 82.6, 118, 169, 241, 344, 491 and 701 μg/mL in the presence and absence of metabolic activation. None of the concentrations caused a significant reduplication in mitotic index. No significant increases in cells with chromosomal aberrations, polyploidy or reduplication were observed. The positive and negative controls responded appropriately. No cytogenetic activity was seen in this assay.
Butyronitrile did not induce chromosomal aberrations in this assay.

Isobutyronitrile (CASRN 78-82-0)
CHO cells were exposed to butyronitrile at 239, 342, 489 and 669 μg/mL without metabolic activation and at 296, 394, 525 and 700 μg/mL with metabolic activation. None of the concentrations caused a significant reduplication in mitotic index. No significant increases in cells with chromosomal aberrations, polyploidy or endo-reduplication were observed. The positive and negative controls responded appropriately. No cytogenetic activity was seen in this assay.
Isobutyronitrile did not induce chromosomal aberrations in this assay.

In vivo

Propionitrile (CASRN 107-12-0)

Male and female Sprague-Dawly rats were administered propionitrile via gavage at 0, 100 and 200 mg/kg-bw. Animals were euthanized at 6, 24 or 48 hours following dosing, femur bones were removed, bone marrow cells were collected, fixed, stained and analyzed for the mean mitotic indices, chromosome numbers, percent aberrant cells and mean number of aberrations per cell. There was no effect of treatment with proponitrile on the frequency of chromosomal aberrations, aberrations per cell, mean chromosome number or mitotic index in comparison to the control animals at any time point. Positive controls resulted in the expected outcome.
Propionitrile did not induce chromosomal aberrations in this assay.

Additional Information

Skin Irritation

New Zealand white rabbits were administered 0.2 mL of propionitrile on to the skin for 24 hours. Slight erythema and edema were noted at the application site at 24 and 48-hour scoring intervals. The irritation was cleared by 72 hours.
Propionitrile was slightly irritating to rabbit skin.

Eye Irritation

New Zealand white rabbits were instilled 0.1 mL of propionitrile into the eye. Severe erythema, very slight edema and copious discharge were seen up to 24 hours. By day 10 all eyes were cleared.
Propionitrile was irritating to rabbit eyes.

Mechanistic Study

Propionitrile (CASRN 107-12-0) and Butyronitrile (CASRN 109-74-0)

(1) Male mice were administered a single dose of propionitrile or butyronitrile via intraperitoneal (i.p.) injection. Mice were divided into 3 groups of 10 animals each. Group 1 received 45 mg/kg-bw i.p. propionitrile only; Group 2 received i.p. injections of 75 mg/kg-bw sodium nitrite (a cyanide antagonist) 20 minutes before and 100 minutes after i.p. injection of 45 mg/kg propionitrile and Group 3 received i.p. injections of 1 g/kg-bw sodium thiosulfate (a cyanide antagonist) 20 minutes before and 80 and 180 minutes after i.p. injection of 45 mg/kg propionitrile. Nine out of 10 mice died in the group treated only with 45 mg/kg propionitrile. Co-treatment with sodium nitrite reduced the mortality to 5 out of 9. None of the 10 animals that were co-treated with sodium thiosulfate died.

(2) Two groups of 10 mice were administered either 0.2 mL of vegetable oil or 0.2 mL of 20% carbon tetrachloride (a hepatotoxic dose) in vegetable oil subcutaneously 24 hours before i.p. treatment with 45 mg/kg propionitrile. In both experiments, animals were observed for 7 days. The mortality rate for animals treated only the 45 mg/kg propionitrile was 8/10 whereas none of the animals co-treated with carbon tetrachloride died.

(3) Concentrations of cyanide in liver and brain were determined in (a) 5 mice treated only with 28 mg/kg-bw propionitrile; (b) 5 mice given 1 g/kg-bw sodium thiosulfate before and after a dose of 28 mg/kg-bw propionitrile; and (c) 5 mice given 0.2 mL of 20% carbon tetrachloride before i.p. treatment with 28 mg/kg-bw propionitrile. All mice were killed 2.5 hours after dosing and propionitrile and cyanide concentrations were determined in the livers and brains. Cyanide concentrations in liver and brain of mice treated with propionitrile alone were markedly greater than mice co-treated with sodium thiosulfate or carbon tetrachloride.

These studies indicate that propionitrile is activated by the liver to release cyanide, which is responsible for the acute effects observed that are associated with cyanide toxicity. Similar results were obtained from studies with butyronitrile.

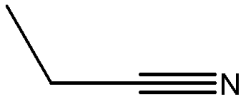
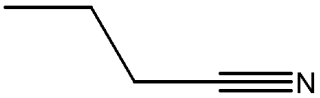
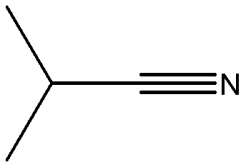
Conclusion: Acute toxicity of alkyl nitriles category members is high via oral and dermal and moderate via inhalation routes. Results of mechanistic studies indicate that propionitrile and butyronitrile are activated by the liver to release cyanide, which is responsible for acute effects observed that are associated with cyanide toxicity. Systemic toxicity is high following repeated oral and inhalation exposures in rats in the repeated-dose toxicity studies with propionitrile. No effects were seen on reproductive parameters in male and female fertility studies via inhalation or on reproductive organs in the repeated-dose toxicity studies with propionitrile. Prenatal developmental toxicity study in rats with propionitrile via oral route showed high maternal and developmental toxicity. However, prenatal developmental studies in rats with butyronitrile and isobutyronitrile via inhalation showed moderate developmental toxicity. The category members did not induce gene mutation or chromosomal aberrations. Propionitrile was irritating to rabbit eyes and slightly irritating to rabbit skin.

Table 3. Summary of Health Effects Data			
Endpoints	**Propionitrile (107-12-0)**	**Butyronitrile (109-74-0)**	**Isobutyronitrile (78-82-0)**
Acute Oral Toxicity LD_{50} (mg/kg-bw)	**40 – 270**	**50 – 111**	**50 – 100**
Acute Dermal Toxicity LD_{50} (mg/kg-bw)	**40 – 90**	**398**	**239**
Acute Inhalation Toxicity LC_{50} (mg/L)	**3.3**	**> ~ 3.4 (1 h)**	**> ~ 3.4 (1 h)**
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	**NOAEL = 1.34 LOAEL = 3.72**	No Data NOAEL = 1.34 LOAEL = 3.72 (RA)	No Data NOAEL = 1.34 LOAEL = 3.72 (RA)
Repeated-Dose Toxicity NOAEL/LOAEL Inhalation (mg/L/day)	**NOAEL = Not established LOAEL ~ 0.135**	No Data NOAEL = Not established LOAEL = 0.135 (RA)	No Data NOAEL = Not established LOAEL = 0.135 (RA)
Reproductive Toxicity NOAEL/LOAEL Inhalation (mg/L/day)	**NOAEL ~ 0.47** (hdt)	No Data NOAEL ~ 0.47 (hdt) (RA)	No Data NOAEL ~ 0.47 (hdt) (RA)
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-bw-day)		–	–
Maternal toxicity	**NOAEL = 40 LOAEL = 80**		
Developmental Toxicity	**NOAEL = 20 LOAEL = 40**		
Developmental Toxicity NOAEL/LOAEL Inhalation (mg/L/day)	–		
Maternal toxicity		**NOAEL ~ 0.56** (hdt)	**NOAEL ~ 0.28 LOAEL ~ 0.56**
Developmental Toxicity		**NOAEL ~ 0.42 LOAEL ~ 0.56**	**NOAEL ~ 0.28 LOAEL ~ 0.56**
Genetic Toxicity – Gene Mutation *In vitro*	**Negative**	**Negative**	**Negative**
Genetic Toxicity – Chromosomal Aberrations *In vitro*	No Data Negative (RA)	**Negative**	**Negative**
Genetic Toxicity – Chromosomal Aberrations *In vivo*	**Negative**	No Data Negative (RA)	No Data Negative (RA)

Table 3. Summary of Health Effects Data			
Endpoints	**Propionitrile (107-12-0)**	**Butyronitrile (109-74-0)**	**Isobutyronitrile (78-82-0)**
Other Information		–[1]	–[1]
Skin Irritation	Slightly irritating		
Eye Irritation	Irritating		

Measured data in bold text; RA = Read Across; hdt = highest dose tested; – endpoint addressed; –[1]data not needed

Table 4

SPONSORED CHEMICALS		
Chemical Name	**CASRN**	**Chemical Structure**
Propanenitrile	107-12-0	
Butanenitrile	109-74-0	
Propanenitrile, 2-methyl-	78-82-0	

Appendix B: Screening Level Exposure Characterization

CHEMICAL CATEGORY NAME
Alkyl Nitriles

SPONSORED CHEMICALS

Propionitrile (CASRN 107-12-0)
[CA Index Name: Propanenitrile]

Butyronitrile (CASRN 109-74-0)
[CA Index Name: Butanenitrile]

Isobutyronitrile (CASRN 78-82-0)
[CA Index Name: Propanenitrile, 2-methyl-]

This exposure characterization was completed using both public, non-confidential sources, and one or more IUR submissions that were available as of this writing.

Volume and Use Information

The three chemicals in the alkyl nitriles category had aggregated production and/or import volumes in the United States between 3 million and 30 million pounds in calendar year 2005. Non-confidential information in the IUR indicates that these chemicals were manufactured and/or imported at the following companies: Solutia Inc. (CASRN 107-12-0) and Eastman Chemical Company (CASRN 109-74-0 and 78-82-0). There may be other companies that are claimed confidential. Persons submitting IUR information for 2005 asserted that some or all of the information was confidential. Only non-confidential versions of reported IUR data are included in this summary.

Table 1 for each chemical at the end of this summary lists the non-confidential industrial processing and uses from IUR submissions. No commercial and consumer uses are reported in IUR submissions as shown in Table 2 for each chemical.

The HPV submission for the alkyl nitriles category states that all three chemicals are primarily used as intermediates that are chemically converted to other chemicals.

Information from the HSDB indicates that CASRN 107-12-0 is used as a chemical intermediate to manufacture di-n-propylamine and cyanoacetates, as a solvent in petroleum refining, as raw material for drug manufacture, and as dielectric fluid. The HSDB information for CASRN 109-74-0 indicates that the chemical is used as basic material in chemical and pharmaceutical intermediates and products, and in poultry medicines. Pharmaceutical and medical products are

not TSCA uses and are not characterized in this report. CASRN 78-82-0 is used as intermediate for insecticides, and as a catalyst in the polymerization of ethylene, in organic synthesis.[6] Additional research indicated that this chemical is not currently used as a gasoline additive.

Environmental Releases

Environmental releases may impact general population and environmental exposures. Factors affecting releases include volumes produced, processed and used; numbers of sites; and processes of manufacture, processing, and use.

Based on IUR data, the maximum total numbers of industrial sites manufacturing, processing, or using these chemicals are confidential.

The following release statements are made based on inferences regarding the non-confidential use information reported in IUR.

Many chemicals designated to be reactants/ chemical intermediates have industrial releases that are a relatively low percentage of the volume. Lower percentage releases occur when a high percentage of the chemical reacts without excess loss during its use as an intermediate. The actual percentages and quantities of releases of the reported chemicals associated with these processing or uses are not known.

The chemicals are not on the Toxics Release Inventory.[7]

Experience has shown that air releases due to volatilization have not been an issue for chemicals with vapor pressures below 0.01 mm Hg. These chemicals' vapor pressures of 20 to 47 mm Hg could result in significant air releases.

Exposures to the General Population and the Environment

Based on the information under the release section above, there may be potential for releases to air during manufacturing, processing, and use. A search of additional relevant databases did not provide any further information on releases of this chemical.

Persistence and bioaccumulation ratings for the alkyl nitriles chemicals are P1 and B1. These ratings suggest that alkyl nitriles are not persistent in the environment; and are not bioaccumulative. The alkyl nitriles are liquids with high water solubility and high vapor pressure.

Based on the information considered including environmental fate, known uses, and the Agency's expert judgment, EPA identifies, for purposes of risk-based prioritization, a low

[6] HSDB, 2008. Hazardous Substances Data Bank. Accessed, 8/11/08, Alkyl Nitrile Category. http://toxnet.nlm.nih.gov.
[7] USEPA, 2006. Toxic Release Inventory. Accessed, 8/11/08. http://www.epa.gov/triexplorer/

potential that the general population and the environment might be exposed to the alkyl nitriles category chemicals.

Exposures to Workers

Worker exposures may be impacted by many factors, including but not limited to volumes produced, processed and used; physical forms and concentrations; processes of manufacture, processing, and use; chemical volatility, and exposure controls, such as engineering controls and personal protective equipment.

Based on IUR data, the maximum total number of workers reasonably likely to be exposed to these chemicals during manufacturing and industrial processing and use may be between 100 and 999 for CASRN 107-12-0 and less than 100 for each of CASRN 109-74-0 and 78-82-0. There may be additional potentially exposed industrial workers who are not included in this estimate. This estimate does not include potentially exposed commercial workers.

The National Occupational Exposure Survey (NOES) has no data for total number of workers potentially exposed to these alkyl nitriles chemicals under the CASRN 107-12-0, 109-74-0 and 78-82-0.[8]

Based on IUR data, all three alkyl nitriles chemicals are manufactured in liquid form, and worker exposures are possible for these chemicals in this form. There may be other physical forms that are claimed confidential. Also, the non-confidential maximum concentration is up to 100%. There may be other concentrations that are claimed confidential.

Propanenitrile has a vapor pressure of 40 mm Hg. Butanenitrile has a vapor pressure of 20 mm Hg. Propanetrile, 2-methyl- has a vapor pressure of 47 mm Hg. Experience has shown that worker exposures to vapors have not been an issue for chemicals with vapor pressures below 0.001 mm Hg. These chemicals' vapor pressures could result in significant worker exposures to vapors if workers are near to the open liquid.

The alkyl nitriles category chemicals do not have OSHA Permissible Exposure Limits (PELs).[9]

Based on the information considered (including IUR data and information from HPV submission), and in combination with the Agency's professional judgment, EPA identifies, for the purposes of risk-based prioritization, a high relative ranking for potential worker exposure for the category chemicals. The rankings are primarily based on the high vapor pressures of these chemicals.

[8] NIOSH, 1983. National Occupational Exposure Survey (NOES, 1981-1983). Accessed, 8/11/08. http://www.cdc.gov/noes/

[9] NIOSH, 1988. OSHA PEL Project Documentation. http://www.cdc.gov/niosh/pel88/npelcas.html Accessed, 8/11/08.

Exposures to Consumers

IUR submissions did not include consumer uses.

EPA identifies, for the purposes of risk-based prioritization, a low potential that consumers might be exposed to the alkyl nitriles category chemicals because they are not reported to be present in consumer products in any of the sources searched.

Exposures to Children

EPA identifies, for the purposes of risk-based prioritization, a low potential that children might be exposed to the alkyl nitriles category chemicals based on no uses specifically intended for children being identified from any source and that the category chemicals are not present in consumer products.

Non Confidential IUR Data Summary: CASRN 107-12-0

Manufacturing/Import Information

Production (including import) volume:	1 million to 10 million pounds
List of non-CBI companies*:	Solutia Inc
Maximum number of potentially exposed workers**:	between 100 and 999
Highest non-CBI maximum concentration*:	up to 100%
Non-CBI physical forms*:	liquid

* There may be other companies, concentrations and physical forms that are claimed confidential.
** Includes all manufacturing and industrial processing and use workers. There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information

Processing Activity	Industrial Sector	Function in Industrial Sector
One or more items may have been claimed as confidential.		

Table 2
Commercial/ Consumer Uses

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
None reported		

Non Confidential IUR Data Summary: CASRN 109-74-0

Manufacturing/Import Information

Production (including import) volume:	1 million to 10 million pounds
List of non-CBI companies *:	Eastman Chemical Company
Maximum number of potentially exposed workers**:	less than 100
Highest non-CBI maximum concentration*:	up to 100%
Non-CBI physical forms*:	liquid

* There may be other companies/ sites, concentrations and physical forms that are claimed confidential.
** Includes all manufacturing and industrial processing and use workers. There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information

Processing Activity	Industrial Sector	Function in Industrial Sector
Processing as a reactant	Other Basic Organic Chemical Manufacturing	Intermediates
One or more items may have been claimed as confidential.		

Table 2
Commercial/ Consumer Uses

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
None reported		

Non Confidential IUR Data Summary: CASRN 78-82-0

Manufacturing/Import Information

Production (including import) volume:	1 million to 10 million pounds
List of non-CBI companies *:	Eastman Chemical Company
Maximum number of potentially exposed workers**:	less than 100
Highest non-CBI maximum concentration*:	up to 100%
Non-CBI physical forms*:	liquid

* There may be other companies, concentrations and physical forms that are claimed confidential.
** Includes all manufacturing and industrial processing and use workers. There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information

Processing Activity	Industrial Sector	Function in Industrial Sector
Processing as a reactant	Other Basic Organic Chemical Manufacturing	Intermediates
One or more items may have been claimed as confidential.		

Table 2
Commercial/ Consumer Uses

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
None reported		