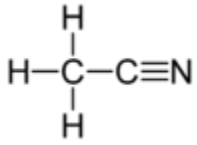
CAS Number: 75-05-8

QCAT Evaluation:
Author: Leatta Dahlhoff
Title: Toxics Reduction Specialist
Organization: WA State Dept. Ecology
Date: 7/28/2016

Peer Review:
Reviewer: Alex Stone
Title: Safer Chemical Alternative Chemist
Organization: HWTR
Date: 5 January 2017

QCAT Chemical Assessment

Chemical Name:	Acetonitrile
CAS #:	75-05-8
Also Called:	Acetonitril; Cyanomethane; Cyanure de methyl; Ethanenitrile; Ethyl nitrile; Methanecarbonitrile; Methane, cyano-; Methylkyanid; NCI-C60822; RCRA waste number U003; USAF EK-488
Identify Applications/Functional Uses:	It is produced mainly as a byproduct of acrylonitrile manufacture. It is used as a polar aprotic solvent in organic synthesis and in the purification of butadiene.
Molecular Formula:	C_2H_3N
Molecular Weight:	41.05 g/mol
Chemical Structure:	

Hazard Summary Table:

Human Health Group 1 (HH1)					Human Health Group 2 (HH2)							Ecological			Fate		Physical	
C	M	R	D	E	AT	ST	N	SnS	SnR	IrS	IrE	AA	CA	E_o	P	B	Ex	F
M	L	L	M	DG	L							L			M	vL		

Note: Please see Appendix A for glossary of hazard endpoint acronyms.

Grades		
Initial	**Data Gap**	**Final**
B	**B**	**B**

Although data was limited for some hazard endpoints, a level of concern could be assigned to acetonitrile for eight of the nine QCAT hazard endpoints. Based upon this data, acetonitrile was identified as an initial Grade B based on carcinogenicity and developmental toxicity due to listings by US EPA as a Group D carcinogen. In addition, the initial Grade B was given for the very low score for the bioaccumulation endpoint, as there were three Step 2 sources for acetonitrile and all identified a low or very low level of concern. Using QCAT grading criteria, acetonitrile was assigned a Grade B as only one data gap for endocrine activity exists, and does not change the final grade. Therefore a final Grade of B was assigned to acetonitrile.

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The Pharos database was accessed on July 28, 2016 and used to research all Step 1 sources.

Human Health Effects – Group I

Carcinogenicity (C) Hazard Level (H, M, L or DG): M

Research Summary:

Limited data was available on the carcinogenicity of acetonitrile for all QCAT sources. EPA IRIS indicated the compound was not classifiable for carcinogenicity. EPA IRIS Group D equates to a moderate (M) level of concern using the QCAT criteria. RTECS indicates there was equivocal evidence it is a tumorigenic agent. Based upon this limited information, acetonitrile was assigned a MODERATE (M) level of concern. Additional data may greatly impact this determination.

References:

- **US EPA**-IRIS Carcinogens-(1986) Group D-Not classifiable as to human carcinogenicity
- **RTECS-**

Type of Test	Route of Exposure or Administration	Species/Test System	Dose Data	Toxic Effects
TCLo - Lowest published toxic concentration	Inhalation	Rodent - rat	400 ppm/6H/2Y (intermittent)	Tumorigenic - equivocal tumorigenic agent by RTECS criteria Liver - tumors

Mutagenicity and Genotoxicity (M) Hazard Level (H, M, L or DG): L

Research Summary: Secondary source data available in Step I source.

The majority of data reported suggest a low level of concern. HSBD indicate the compound was not found to cause negative effects in other genetic studies except chromosome loss in yeast. And it shows that the compound is neither clastogenic nor aneugenic. A **clastogen** in biology is a mutagenic agent giving rise to or inducing disruption or breakages of chromosomes, leading to sections of the chromosome being deleted, added, or rearranged. An aneugen is a substance that causes a daughter cell to have an abnormal number of chromosomes or aneuploidy. A substance's aneugenicity reflects its ability to induce aneuploidy. There was one Step I Secondary source that noted a moderate level of concern. However, the evaluator has deemed the studies noted in HSDB more representative of the level of concern.

Tests for mutagenicity were also negative. Negative results were also obtained in a reverse mutation assay. Based upon this information, a LOW (L) level of concern was assigned to acetonitrile.

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References:

Step I Secondary source:

Japan-GHS- Germ cell mutagenicity-Category 2 - **M**

Step II Sources

- **HSDB:**

0.2.22 GENOTOXICITY

A) **Acetonitrile** caused chromosome loss in yeast, but was not found to cause negative effects in other genetic studies.

/GENOTOXICITY/ **Acetonitrile** was tested for its ability to induce clastogenic or aneugenic effects through the induction of micronucleated polychromatic erythrocytes (MNPCE) in mouse bone marrow and peripheral blood. Groups of NMRI mice, five males and five females, were administered a single i.p. dose of **acetonitrile**, corresponding to the maximum tolerated dose (MTD), 100 or 125 mg/kg body wt for males and females, respectively. Bone marrow was sampled at 18, 24 or 36 hr after treatment, while peripheral blood was sampled before and 24, 48, 72 and 96 hr after treatment. Positive controls were administered cyclophosphamide (65 mg/kg i.p.). **Acetonitrile** did not increase the incidence of MNPCE in either bone marrow or peripheral blood in male mice or in peripheral blood in females. A small, but statistically significant (P: < 0.05), increase was observed in female bone marrow 36 hr after administration, but since this was within the range of the control data it is not considered to be of biological significance. Cyclophosphamide increased the incidence of MNPCE in bone marrow and peripheral blood of both sexes. It is concluded that acetonitrile **is neither clastogenic nor aneugenic** in the bone marrow of the mouse at the MTD.

/GENOTOXICITY/ **Acetonitrile** was **tested for mutagenicity** in the Salmonella/microsome preincubation assay using the standard protocol approved by the National Toxicology Program. **Acetonitrile** was tested at doses of 0.10, 0.33, 1.0, 3.3, and 10 mg/plate in as many as 5 Salmonella typhimurium strains (TA1535, TA1537, TA97, TA98, and TA100) in the presence and absence of rat or hamster liver S-9. **Acetonitrile was negative** in these tests and the highest ineffective dose tested in any Salmonella typhimurium strain was 10 mg/plate.

/GENOTOXICITY/ **Negative results** were obtained in a preincubation S. typhimurium assay and a reverse **mutation assay** in Saccharomyces cerevisiae D7, conducted in the presence and absence of S9 from rats induced with **acetonitrile** or phenobarbitone, although the bacterial assay was limited by the use of stationary cultures.

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Reproductive Toxicity (R) Hazard Level (H, M, L or DG): L

Research Summary: Two sources (RTECS and HSDB) identified acetonitrile had low reproductive toxicity. There were no Step 1 sources available. Step two sources equate to a LOW L level of concern using the QCAT criteria. Several studies noted in HSDB showed no reproductive impact including no effects in fetal rats, no changes in pregnancy, etc.

References:

- HSDB:

  /LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ Rats were exposed 6 hours/day by inhalation at 100, 400, or 1200 ppm from gestational day 6 to 19; the fetal status was then determined. **One rat died at 400 and two at 1200 ppm**...**No effects were seen in the fetal rats**…Rats exposed at a range of concentrations from 900 to 1800 ppm showed embryo lethality (early resorptions) at the 1800 ppm concentration. Female rats given oral doses of 300 or 500 mg/kg, which produced measurable toxicity in most of the females, showed no changes in pregnancy rates, resorption of litters, or perinatal toxicity to the offspring.

  /LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ Rats were given gavage doses of 125, 190, or 275 mg **acetonitrile**/kg from gestational days 6 through 19…**There were no structural abnormalities in the fetuses derived from acetonitrile-exposed rats.**..

- RTECS-

Type of Test	Route of Exposure or Administration	Species/Test System	Dose Data	Sex/Duration	Toxic Effects
TCLo - Lowest published toxic concentration	Inhalation	Rodent - rat	1800 ppm/6H	female 6-20 day(s) after conception	Reproductive - Fertility - post-implantation mortality (e.g. dead and/or resorbed implants per total number of implants)
TDLo - Lowest published toxic dose	Oral	Rodent - rabbit	390 mg/kg	female 6-18 day(s) after conception	Reproductive - Maternal Effects - other effects Reproductive - Effects on Embryo or Fetus - fetal death Reproductive - Specific Developmental Abnormalities - musculoskeletal system

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TDLo - Lowest published toxic dose	Oral	Rodent - hamster	300 mg/kg	female 8 day(s) after conception	Reproductive - Specific Developmental Abnormalities - musculoskeletal system
TDLo - Lowest published toxic dose	Oral	Rodent - hamster	400 mg/kg	female 8 day(s) after conception	Reproductive - Fertility - post-implantation mortality (e.g. dead and/or resorbed implants per total number of implants)
TCLo - Lowest published toxic concentration	Inhalation	Rodent - hamster	5000 ppm/1H	female 8 day(s) after conception	Reproductive - Fertility - post-implantation mortality (e.g. dead and/or resorbed implants per total number of implants) Reproductive - Specific Developmental Abnormalities - Central Nervous System
TCLo - Lowest published toxic concentration	Inhalation	Rodent - hamster	8000 ppm/1H	female 8 day(s) after conception	Reproductive - Effects on Embryo or Fetus - fetotoxicity (except death, e.g., stunted fetus) Reproductive - Specific Developmental Abnormalities - musculoskeletal system
TDLo - Lowest published toxic dose	Oral	Rodent - rat	2 mg/kg	female 10 day(s) after conception	Reproductive - Effects on Embryo or Fetus - other effects to embryo

Development Toxicity incl. Developmental Neurotoxicity (D) Hazard Level (H, M, L or DG): M

Research Summary:

Data on developmental toxicity is limited. Acetonitrile is identified by one authoritative source, MAK Commission of Germany (Deutsche Forschungsgemeinschaft), as a pregnancy risk group C, which is assigned a MODERATE (**M**) level of concern. As there is only one data point used for this determination, additional data may impact the level of concern assigned.

References:

Pharos:

- **MAK Commission of Germany (Deutsche Forschungsgemeinschaft)** pregnancy risk group C. There is no reason to fear damage to the embryo or fetus when MAK and BAT values are observed.

Endocrine Disruption (E) Hazard Level (H, M, L or DG): DG

Research Summary:

No data found via Step I or Step II sources. Therefore a level of concern of DATA GAP (**DG**) was assigned.

References: No data found.

Human Health Effects – Group II

Acute Mammalian Toxicity (AT) Hazard Level (vH, H, M, L or DG): M

Research Summary:

Numerous and conflicting data exist for this endpoint. The European Union has assigned hazard and risk phrases that indicate a moderate level of concern using QCAT criteria. Several governments (New Zealand, Japan, Quebec and Malaysia) have identified levels of concern ranging from low to very high. QCAT, however, identified the EU hazard and risk phrases as a primary data source and the government lists as secondary sources; therefore, the determination by the EU as a priority source is used to assign a MODERATE (**M**) level of concern for this endpoint.

References:

- **Pharos**

  STEP 1 Priority sources:
  - EU - R-phrases - R20 - Harmful by Inhalation (gas or vapor or dust/mist): M
  - EU - GHS (H-Statements) - H302 - Harmful if swallowed: M
  - EU - GHS (H-Statements) - H312 - Harmful in contact with skin: M
  - EU - GHS (H-Statements) - H332 - Harmful if inhaled: M
  - EU - R-phrases - R21 - Harmful in Contact with Skin: M
  - EU - R-phrases - R22 - Harmful if Swallowed: M

  STEP 1 Secondary sources
  - Québec CSST - WHMIS 1998 - Class D2B - Toxic material causing other toxic effects
  - New Zealand - GHS - 6.1C (dermal) - Acutely toxic: H

- New Zealand - GHS - 6.1C (inhalation) - Acutely toxic: H
- Japan - GHS - Acute toxicity (dermal) - Category 3: H
- Japan - GHS - Acute toxicity (oral) - Category 5: L
- Québec CSST - WHMIS 1998 - Class D1A - Very toxic material causing immediate and serious toxic effects: vH
- New Zealand - GHS - 6.1B (oral) - Acutely toxic: vH

Environmental Health Effects

Acute Aquatic (AA) Toxicity Hazard Level: (vH, H, M, L or DG): L

Research Summary:

No Step 1 sources available. There was an abundance of evidence for fish, crustacea, algae or other aquatic plants with values falling in the low level of concern. Based upon data from Step II sources, a **LOW (L)** level of concern for aquatic toxicity using QCAT chemical ranking was assigned.

References:

- **ECOTOX**

Spec. Sci. Name Spec. Common Name	Exp. Type Chem. Anal.	Media Type Loc	Resp. Site Obs. Dur. (Days)	Endpoint BCF	Trend Eff %	Effect Effect Meas.	Conc. Type Conc. (Std) Appl. Rate
Pimephales promelas Fathead Minnow	S U	FW LAB	4 d	LC50*		MOR MORT	A 1000000 ug/L
Pimephales promelas Fathead Minnow	F M	FW LAB	4 d	LC50		MOR MORT	A 1640000 (1600000-1690000) ug/L

Environmental Fate

Persistence (P) Hazard Level: (vH, H, M, L, vL or DG): M

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Research Summary:

Numerous and conflicting data exist for this endpoint. The Canadian DSL has identified acetonitrile as persistent which equates to very high level of concern. The PBT Profiler ranges from very high for air, medium for soil, and low for water. However PBT Profiler predicts that acetonitrile partitions 40% to water and 48% to soil. HSDB reported values of very high for atmospheric degradation. Based on this information, acetonitrile is given a MODERATE (**M**) level of concern for this endpoint due to 48% partitioning to soil and it was the average value of the range of levels identified.

References:

- **Pharos**-

Step 1 Secondary source:

EC-CEPA DSL-Persistent Notes potential hazard concern in Pharos.

Step 2 sources:

- **PBT Profiler**

Persistence | Bioaccumulation

75-05-8 Acetonitrile

PBT Profiler Estimate = PBT

Media	Half-Life (days)	Percent in Each Medium	BCF
Water	15	40%	3.2
Soil	30	48%	
Sediment	140	0%	
Air	67	12%	

- **HSDB:**

Vapor-phase **acetonitrile** will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 610 days. Vapor-phase **acetonitrile** will also be degraded in the atmosphere by reaction with ozone; the half-life for this reaction in air is estimated to be greater than or equal to 76 days.

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Bioaccumulation (B) Potential Hazard Level: (vH, H, M, L, vL or DG): vL

Research Summary:

There were three Step 2 sources for acetonitrile and all identified a low or very low level of concern. Therefore acetonitrile was assigned a very LOW (**vL**) level of concern.

References:

- **UNEP SIDS**-Acetonitrile is considered readily biodegradable...
- **HSDB-** AQUATIC FATE: …**BCF of 3** …**log Kow of -0.34**… **potential for bioconcentration in aquatic organisms is low…**
- **BPT Profiler:**