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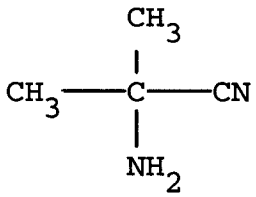
Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as additional references at the end of each appropriate section, with a statement to reflect the reason why these studies were not summarized.

1.0 Substance Information

CAS Number: 19355-69-2

Chemical Name: Propanenitrile, 2-amino-2-methyl-

Structural Formula:



Other Names:
α-Amino-α-methylpropionitrile
α-Aminoisobutyronitrile
1-Cyano-1-methylethylamine
2-Amino-2-cyanopropane
2-Amino-2-methylpropanenitrile
2-Amino-2-methylpropionitrile
2-Aminoisobutyronitrile
2-Aminopropane-2-carbonitrile
2-Cyanoisopropylamine
ABN
ACAN
Aminodimnethylacetonitrile
Vazo 64AN

Exposure Limits: 5 ppm (15-minute TWA), skin: DuPont Acceptable Exposure Limit (AEL)

2.0 Physical/Chemical Properties

2.1 Melting Point

Value: - 4.7°C
Decomposition: No Data
Sublimation: No Data
Pressure: 760 mm Hg
Method: Modeled. MPBPWIN, v.1.41, module of EPIWIN 3.11 (Syracuse Research Corporation). MPBPWIN estimates melting point by 2 different methods. The first is an

	adaptation of the Joback group contribution method for melting point (Joback, 1982; Reid et al; 1987) and the second is a simple Gold and Ogle method suggested by Lyman (1985).
GLP:	Not Applicable
Reference:	Joback, K. G. (1982). A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques, Stevens Institute of Technology, submitted to the Dept. of Chem. Eng. for M.S. Degree at the Massachusetts Institute of Technology in June 1984 (see also: Reid et al., 1987). Reid, R. C. et al. (1987). The Properties of Gases and Liquids, 4th edition, Chapter 2, McGraw-Hill, Inc., NY. Lyman, W. J. (1985). In: Environmental Exposure From Chemicals, Volume I, Chapter 2, Neely, W. B. and G. E. Blau (eds.), CRC Press, Inc., Boca Raton, FL.
Reliability:	Estimated value based on accepted model.

Additional Reference for Melting Point:

DuPont Co. (1999). Material Safety Data Sheet 1009CR (March 12).

2.2 Boiling Point

Value:	No Data
Decomposition:	Yes
Pressure:	No Data
Method:	No Data
GLP:	Unknown
Reference:	DuPont Co. (1999). Material Safety Data Sheet DU000540 (March 12).
Reliability:	Not assignable because limited study information was available.

Additional Reference for Boiling Point:

Degussa Corp. (1985). Material Safety Data Sheet (October).

2.3 Density

Value:	Specific gravity = 0.9
Temperature:	25°C
Method:	No Data
GLP:	Unknown
Results:	No additional data.
Reference:	DuPont Co. (1999). Material Safety Data Sheet 1009CR (March 12).
Reliability:	Not assignable because limited study information was available.

Additional Reference for Density:

Degussa Corp. (1985). Material Safety Data Sheet (October).

2.4 Vapor Pressure

Value:	30 mm Hg
Temperature:	66°C
Decomposition:	No Data
Method:	No Data
GLP:	Unknown
Reference:	DuPont Co. (1999). Material Safety Data Sheet 1009CR (March 12).
Reliability:	Not assignable because limited study information was available.

Value:	2.84
Temperature:	25°C
Decomposition:	No Data
Method:	Estimated as the mean of Antoine & Grain methods
GLP:	Not Applicable
Reference:	SRC MPBPWIN v1.40 in EPIWIN v3.11. Syracuse Research Corporation (MPBPWIN) program estimates the vapor pressure using the modified Grain method. A description of the methodology is detailed in: Lyman, W. J. (1985). In: Environmental Exposure From Chemicals, Volume I, Chapter 2, Neely, W. B. and G. E. Blau (eds.), CRC Press, Inc., Boca Raton, FL.
Reliability:	Estimated value based on accepted model.

Additional Reference for Vapor Pressure:

Degussa Corp. (1985). Material Safety Data Sheet (October).

2.5 Partition Coefficient (log Kow)

Value:	-0.04 (SMILES: C(#N)C(N)(C)C) -3.23 (SMILES: C(#N)C(N(H)(H)(H)(CL))(C)C) as ionized salt at acidic environmental pH and high dilution
Temperature:	25°C
Method:	Modeled. KOWWIN, v. 1.67, module of EPIWIN 3.11 (Syracuse Research Corporation). KOWWIN uses "fragment constant" methodologies to predict log P. In a "fragment constant" method, a structure is divided into fragments (atom or larger functional groups) and coefficient values of each fragment or group are summed together to yield the log P estimate.
GLP:	Not Applicable
Reference:	Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci., 84:83-92.
Reliability:	Estimated value based on accepted model.

Additional References for Partition Coefficient (log Kow): None Found.

2.6 Water Solubility

Value:	Soluble at greater than 100 g/L
Temperature:	No Data
pH/pKa:	pKa = 4.9
Method:	Modeled. Solubility - WSKOWWIN v.1.41, module of EPIWIN 3.11 (Syracuse Research Corporation). Water solubility is estimated from log Kow using molecular weight and molecular fragment correction factors. pKa – SPARC On-line calculator, University of Georgia
GLP:	Not Applicable
Reference:	Solubility - Meylan, W. M. et al. (1996). Environ. Toxicol. Chem., 15:100-106. pKa - http://ibmlc2.chem.uga.edu/sparc/index.cfm
Reliability:	Estimated value based on accepted model.

Additional References for Water Solubility:

Degussa Corp. (1985). Material Safety Data Sheet (October).

DuPont Co. (1999). Material Safety Data Sheet 1009CR (March 12).

2.7 Flash Point

Value:	1.7°C
Method:	SFCC
GLP:	Unknown
Reference:	DuPont Co. (1999). Material Safety Data Sheet 1009CR (March 12).
Reliability:	Not assignable because limited study information was available.

Additional Reference for Flash Point:

Degussa Corp. (1985). Material Safety Data Sheet (October).

2.8 Flammability

Results:	Flammable liquid
Method:	No Data
GLP:	Unknown
Reference:	DuPont Co. (1999). Material Safety Data Sheet 1009CR (March 12).
Reliability:	Not assignable because limited study information was available.

Additional References for Flammability: None Found.

3.0 Environmental Fate

3.1 Photodegradation

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	No Data
Indirect Photolysis:	Estimated half-life = 48 days, due to OH radical oxidation in the atmosphere. With an estimated vapor pressure of 2.84 mm Hg (25°C) 2-amino-2-methylpropanenitrile will exist as a vapor in the atmosphere.
Breakdown Products:	No Data
Method:	Modeled
GLP:	Not Applicable

Reference: Indirect Photolysis: AOPWIN, v.1.91 module of EPIWIN 3.11. Meylan, W. M. and P. H. Howard (1993). Chemosphere, 26:2293-2299.

Reliability: Estimate based on known qualitative structure-activity relationships.

Additional References for Photodegradation: None Found

3.2 Stability in Water

Concentration: No Data

Half-life: In the presence of water and the absence of excess ammonia, aminonitriles may disproportionate into their constituents: ketone, cyanide, and ammonium (Kirk-Othmer, 1978)

% Hydrolyzed: No Data

Method: Modeled. HYDROWIN, v. 1.67 module of EPIWIN v3.11 (Syracuse Research Corporation). HYDROWIN cannot estimate a hydrolysis rate constant for this type of chemical structure.

GLP: Not Applicable

Reference: Kirk-Othmer Encyclopedia of Chemical Technology (1978). 3rd edition, Wiley-Interscience.

Mill, T. et al. (1987). "Environmental Fate and Exposure Studies Development of a PC-SAR for Hydrolysis: Esters, Alkyl Halides and Epoxides," EPA Contract No. 68-02-4254, SRI International, Menlo Park, CA.

Reliability: Estimated value based on accepted model.

Additional References for Stability in Water: None Found

3.3 Transport (Fugacity)

Media: Air, Water, Soil, and Sediments

Distributions:

Compartment	% of total distribution	½ life (hours) (advection + reaction)
Air	1	1150
Water	45.9	900
Soil	53.9	1800
Sediment	0.089	8100

Adsorption Coefficient: Koc =0.374 (calc by model)

Desorption: No Data

Volatility: Henry's Law Constant = 5.54×10^{-9} atm-m^3/mole (HENRYWIN program)

Method: Modeled.

SMILES: C(#N)C(N)(C)C
Molecular Wt: 84.12
Vapor Pressure: 2.84 mm Hg (MPBPWIN program)
Log Kow: -0.04 (KOWWIN program)

Henry's Law Constant - HENRYWIN v. 3.10 module of EPIWIN v3.11 (Syracuse Research Corporation). Henry's Law Constant (HLC) is estimated by two separate methods that yield two separate estimates. The first method is the bond contribution method and the second is the group contribution method. The bond contribution method is able to estimate many more types of structures; however, the group method estimate is usually preferred (but not always) when all fragment values are available.

Koc – Calculated from Kow by the Mackay Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation).

Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v3.11 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments.

GLP: Not Applicable

Reference: HENRYWIN –

J. Hine and P. K. Mookerjee (1975). J. Org. Chem., 40(3):292-298.

Meylan, W. and P. H. Howard (1991). Environ. Toxicol. Chem., 10:1283-1293.

Fugacity - The methodology and programming for the Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation) were developed by Dr. Donald MacKay and coworkers and are detailed in:

Mackay, D. (1991). Multimedia Environmental Models: The Fugacity Approach, pp. 67-183, Lewis Publishers, CRC Press.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1618-1626.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1627-1637.

Reliability: Estimated values based on accepted models.

Additional References for Transport (Fugacity): None Found

3.4 Biodegradation

Value:

Linear Model Prediction:	0.9844 (Biodegrades Fast)
Non-Linear Model Prediction:	0.9971 (Biodegrades Fast)
Ultimate Biodegradation Timeframe:	2.7432 (weeks to months)
Primary Biodegradation Timeframe:	3.5510 (days to weeks)
MITI Linear Model Prediction:	0.6353 (readily degradable)
MITI Non-Linear Model Prediction:	0.6188 (readily degradable)
Breakdown Products:	No Data
Method:	Modeled. BIOWIN, v. 4.01 module of EPINWIN v3.11 (Syracuse Research Corporation). BIOWIN estimates the probability for the rapid aerobic biodegradation of an organic chemical in the presence of mixed populations of environmental microorganisms. Estimates are based upon fragment constants that were developed using multiple linear and non-linear regression analyses.
GLP:	Not Applicable
Reference:	Boethling, R. S. et al. (1994). Environ. Sci. Technol., 28:459-65. Howard, P. H. et al. (1992). Environ. Toxicol. Chem., 11:593-603. Howard, P. H. et al. (1987). Environ. Toxicol. Chem., 6:1-10.

Tunkel, J. et al. (2000). Predicting Ready Biodegradability in the MITI Test. Environ. Toxicol. Chem., 19(10):2478-2485.

Reliability: Estimated value based on accepted model.

Additional References for Biodegradation: None Found

3.5 Bioconcentration

Value: log BCF = 0.5 (unionized or salt)

Method: Modeled. BCFWIN v. 2.15 module of EPINWIN v3.11 (Syracuse Research Corporation). BCFWIN estimates the bioconcentration factor (BCF) of an organic compound using the compound's log octanol-water partition coefficient (Kow) with correction factors based on molecular fragments.

GLP: Not Applicable

Reference: "Improved Method for Estimating Bioconcentration Factor (BCF) from Octanol-Water Partition Coefficient", SRC TR-97-006 (2nd Update), July 22, 1997; prepared for Robert S. Boethling, EPA-OPPT, Washington, DC, Contract No. 68-D5-0012; prepared by William M. Meylan, Philip H. Howard, Dallas Aronson, Heather Printup, and Sybil Gouchie, Syracuse Research Corp.

Reliability: Estimated value based on accepted model.

Additional References for Bioconcentration: None Found

4.0 Ecotoxicity

4.1 Acute Toxicity to Fish

Type: **96-Hour LC_{50}**

Species: *Pimephales promelas*, fathead minnow

Value: 0.71 mg/L

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The test substance was tested in an unaerated, static acute test. Nominal concentrations of the test substance were 0, 0.5, 1.0, 50, 500, and 5000 mg/L. One test chamber per concentration with 5 animals per test chamber were used. The photoperiod was 16 hours light:8 hours dark. Dissolved oxygen and pH were measured in the 0, 0.5, 50, and 5000 mg/L nominal concentrations. No information regarding hardness, alkalinity, TOC, or TSS of the dilution water chemistry was reported.

GLP:	No
Test Substance:	2-Amino-2-methylpropanenitrile, purity 74%
Results:	Mortality was 0, 0, 100, 100, 100, and 100% at 0, 0.5, 1.0, 50, 500, and 5000 mg/L, respectively. Based on visual observations, the test substance was soluble in well water at all but the 5000 mg/L test concentration, which had a slightly cloudy appearance. The dissolved oxygen at 0 and 96 hours or at total mortality in the 0, 0.5, 50, and 5000 mg/L concentrations were 8.6, 8.7, 8.6, and 9.4 mg/L and 7.0, 7.7, 8.6, and 9.4 mg/L, respectively. The pH values at 0 and 96 hours or total mortality were 7.0, 7.1, 8.7, and 9.4 mg/L and 7.3, 7.5, 8.7, and 9.4 mg/L, respectively.
Reference:	DuPont Co. (1992). Unpublished Data, Haskell Laboratory Report No. 788-92, "Static, Acute 96-Hour Screening Test to Fathead Minnows, *Pimephales promelas*" (November 18).
Reliability:	Medium because a suboptimal study design (nominal test concentrations) was used.

Type:	**96-hour LC_{50}**
Species:	Fish
Value:	468.3 mg/L; log Kow = -0.04
Method:	Modeled
GLP:	Not Applicable
Test Substance:	2-Amino-2-methyl propanenitrile
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Fish: None Found.

4.2 Acute Toxicity to Invertebrates

Type:	**48-Hour EC_{50}**
Species:	*Daphnia magna*
Value:	7.1 mg/L
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

	Nominal concentrations used were 0, 0.5, 1.0, 50, 500, and 5000 mg/L. The test chamber was covered with clean glass plates. Two test chambers per concentration were used, with 5 daphnids per test chamber. Dissolved oxygen and pH were recorded at 0 and 48 hours, or at total immobility. No information regarding hardness, alkalinity, TOC, or TSS of the dilution water chemistry was reported.
GLP:	No
Test Substance:	2-Amino-2-methylpropanenitrile, purity 73-75%
Results:	Based on visual observations, the water control solution and the 0.5, 1.0, and 50 mg/L test solutions were clear with no color throughout the study. The 500 and 5000 mg/L test solutions were slightly cloudy at test start. Immobilities were 0, 0, 0, 100, 100, and 100% in the 0, 0.5, 1.0, 50, 500, and 5000 mg/L test concentrations, respectively. Water quality parameters were within acceptable limits, except the pH values in the 50, 500, and 5000 mg/L test solutions at the test start, which were slightly above the maximum limit of 9.0 (range 9.1-9.6), and the dissolved oxygen values in some of the test chambers exceeded the maximum limit of 105% saturation at test temperatures (i.e., approximately 9.7 mg/L at 20°C).
Reference:	DuPont Co. (1998). Unpublished Data, Haskell Laboratory Report No. 1998-01465, "Static, Acute 48-Hour Screening Test to *Daphnia magna*" (March 25).
Reliability:	Medium because a suboptimal study design (nominal test concentrations) was used.

Type:	**48-hour LC_{50}**
Species:	*Daphnia*
Value:	26.6 mg/L; log Kow = -0.04
Method:	Modeled
GLP:	Not Applicable
Test Substance:	2-Amino-2-methyl propanenitrile
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Invertebrates: None Found.

4.3 Acute Toxicity to Aquatic Plants

Type:	**96-hour EC_{50}**
Species:	Algae
Value:	24.8 mg/L; log Kow = -0.04
Method:	Modeled
GLP:	Not Applicable
Test Substance:	2-Amino-2-methyl propanenitrile
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Aquatic Plants: None Found.

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type:	**Oral LD_{50}**
Species/Strain:	Female rats/Charles River Albino
Value:	10-30 mg/kg
Method:	No specific test guideline was reported. An acute oral toxicity study was conducted on female rats (1/dose level), administered undiluted at 0.1 and 1.0% (w/v) aqueous solutions of 3, 10, 30, 100, 300, 1000, 3000, and 10,000 mg/kg. Body weights and clinical signs were periodically recorded. Surviving rats were sacrificed after 14 days. Gross necropsy was performed on all rats.
GLP:	Unknown
Test Substance:	2-Amino-2-methylpropanenitrile, purity not reported
Results:	Rats dosed with 3 or 10 mg/kg survived. Mortality occurred in rats dosed with 30 mg/kg or higher. Death occurred in 1 minute to 1 ¼ hours. The surviving animals at 3 and 10 mg/kg both gained weight over the 14-day observation period. Reactions exhibited by the rats (dose levels 30-10,000 mg/kg) within seconds after oral intubation included hypoactivity, labored breathing, salivation, straub tail, rhinitis, muscular weakness, tremors, fibrillary action, and convulsions. No reactions were noted in animals dosed at the 3 and 10 mg/kg dose levels. Necropsy examination of

the animals that died revealed hemorrhages in the gastrointestinal tracts and dark red lungs. Gastroenteritis was noted at sacrifice in the rat dosed with 3 mg/kg. No other gross pathologic alterations were noted in rats sacrificed at the end of the 14-day observation period.

Reference: Ciba-Geigy Corporation (1974). Study Number 601-05285, "Acute Oral Toxicity Study – Albino Rats" (July 18) (cited in TSCA Fiche OTS0537846).

Reliability: High because a scientifically defensible or guideline method was used.

Additional Reference for Acute Oral Toxicity:

Data from this additional source supports the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

Degussa Corp. (1985). Material Safety Data Sheet (October).

Type: **Inhalation ALC**
Species/Strain: Male rats/Crl:CD®(SD)BR
Exposure Time: 2 or 4 hours
Value: 71 ppm
Method: No specific test guideline was reported.

Groups of 6 male rats each were exposed for 4 hours, whole-body to vapor atmospheres of 22, 32, 46, 65, 71, or 74 ppm. Another group of 6 male rats was exposed whole-body for a single 2-hour period to 74 ppm. Rats were approximately 6-10 weeks old and weighed between 198-365 g at the time of exposure.

Rats were observed for mortality and response to alerting stimuli during the exposure and observed for mortality and clinical signs of toxicity after exposure. During a 14-day post-exposure period, all surviving rats were observed each day for mortality, and were weighed and observed for clinical signs of toxicity at regular intervals. Surviving rats were sacrificed without pathological examination.

Chamber atmospheres were generated by flash evaporation of the test substance in air.

During exposure, rats were placed within wire-mesh cages and exposed whole-body inside the exposure chamber.

	The atmospheric concentration of the test substance was determined by gas chromatography at approximately 30-minute intervals during each exposure. Chamber airflow was set at the beginning of each exposure to achieve at least 12 air changes per hour. Chamber temperature was targeted at 22±2°C. Chamber relative humidity was targeted at 50±10%. Airflow, temperature, and relative humidity were monitored continually.
GLP:	No
Test Substance:	2-Amino-2-methylpropanenitrile, purity 73-75%
Results:	Mortality was 0/6, 0/6, 0/12, 0/6, 6/6, and 5/6 at 22, 32, 46, 65, 71, and 74 ppm, respectively. In general, rats died within 1 day of exposure. Clinical signs of toxicity observed included labored breathing, lethargy, gasping, nasal discharge, and stained fur. No clinical signs of toxicity were observed at ≤ 65 ppm. In general, clinical signs of toxicity were observed for 1-2 days after exposure and had resolved by test day 3. Weight losses of 4-8% were observed in some groups within 1 day of exposure. Rats generally resumed normal weight gains for the remainder of the recovery period.
Reference:	DuPont Co. (1998). Unpublished Data, Haskell Laboratory Report No. 1998-01569, "Inhalation Approximate Lethal Concentration (ALC) in Rats" (July 30) (also cited in TSCA Fiche OTS0590012-1).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Acute Inhalation Toxicity:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1987). Unpublished Data, Haskell Laboratory Report No. 535-87, "One-hour Inhalation Median Lethal Concentration (LC_{50}) Study in Rats" (September 28) (also cited in TSCA Fiche OTS0590012).

Degussa Corp. (1985). Material Safety Data Sheet (October).

Type:	**Dermal ALD**
Species/Strain:	Male rabbits/New Zealand White
Exposure Time:	No Data
Value:	30-100 mg/kg

Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. The test substance was administered undiluted on the abraded skin of rabbits (1/dose level) at doses of 30, 100, 300, 1000, and 3000 mg/kg. Body weights were recorded on days 0, 7, and 14. Gross pathology was performed on all rabbits.
GLP:	Unknown
Test Substance:	2-Amino-2-methylpropanenitrile, purity 76.3%
Results:	Mortality was 0, 100, 100, 100, and 100% at 30, 100, 300, 1000, and 3000 mg/kg, respectively. Death occurred in 10 to 35 minutes. The surviving rabbit given 30 mg/kg gained weight throughout the 14-day observation period. Clinical signs observed at 30 mg/kg included excitation, hypoactivity, dyspnea, ataxia, muscular weakness, mydriasis, and miosis, which lasted from 6 to 22 hours. Clinical signs observed at ≥100 mg/kg included excitation, rapid respiration, hypoactivity, mydriasis, dyspnea, ataxia, muscular weakness, and tonic convulsions. The test substance was slightly to mildly irritating to the skin of the surviving rabbit. Skin changes at 24 hours were characterized by barely perceptible to pale red erythema. At 7 and 14 days, barely perceptible to pale red erythema and slight desquamation were observed at the site of contact. Necropsy examination of the rabbits that died revealed hyperemia and focal hemorrhaging in the lungs. Two rabbits (300 and 3000 mg/kg) exhibited hemorrhaging of the perirenal fat and body wall. No gross pathologic alterations were noted in the rabbit sacrificed at the end of the 14-day observation period.
Reference:	Ciba-Geigy Corporation (1974). Study Number 601-05285, "Acute Dermal Toxicity Study – Albino Rabbits" (July 18) (cited in TSCA Fiche OTS0537842, OTS0543774, and OTS0537846).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Acute Dermal Toxicity: None Found.

Type:	**Dermal Irritation**
Species/Strain:	Male rabbits/New Zealand White

Method:	No specific test guideline was reported. The test substance was administered undiluted on the abraded skin of 1 rabbit at a dose of 30 mg/kg (equivalent to 0.07 g of test substance) for a dermal toxicity study.
GLP:	Unknown
Test Substance:	2-Amino-2-methylpropanenitrile, purity 76.3%
Results:	The test substance was slightly to mildly irritating to the skin. Skin changes at 24 hours were characterized by barely perceptible to pale red erythema. At 7 and 14 days, barely perceptible to pale red erythema and slight desquamation were observed at the site of contact.
Reference:	Ciba-Geigy Corporation (1974). Study Number 601-05285, "Acute Dermal Toxicity Study – Albino Rabbits" (July 18) (cited in TSCA Fiche OTS0537842, OTS0543774, and OTS0537846).
Reliability:	Low because an inappropriate method was used. The volume of test substance was insufficient to accurately assess dermal irritation.

Additional References for Dermal Irritation: None Found.

Type:	**Dermal Sensitization:** No Data.

Type:	**Eye Irritation**
Species/Strain:	Rabbits/Albino
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. The test substance (0.1 mL) was instilled undiluted into the eyes of 3 rabbits. In addition, 1 rabbit was exposed to 0.01 mL of undiluted test substance, and the eye remained unwashed.
GLP:	Unknown
Test Substance:	2-Amino-2-methylpropanenitrile, purity not reported
Results:	Three rabbits dosed with 0.1 mL of the test substance exhibited immediate salivation and convulsions, and died within 5 minutes after instillation of the test substance. The rabbit dosed with 0.01 mL exhibited salivation, muscular weakness, hypoactivity, and diarrhea following instillation of the test substance, and was found dead by 72 hours after instillation. Corneal, iritic, and conjunctival scores were 20, 5, and 12, respectively at 1 and 24 hours following instillation.

Reference:	Ciba-Geigy Corporation (1974). Study Number 601-05285, "Eye Irritation Test – Albino Rabbits" (July 18) (cited in TSCA Fiche OTS0543774 and OTS0537846).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Eye Irritation: None Found.

5.2 Repeated Dose Toxicity

Type:	**Two-Week Inhalation**
Species/Strain:	Male rats/Crl:CD®(SD)BR
Sex/Number:	Male/10 per exposure level
Exposure Period:	2 weeks
Frequency of Treatment:	6 hours/day, 5 days/week
Exposure Levels:	0, 1.4, 7.3, 22 ppm
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Four groups of male rats were exposed whole-body to mean vapor concentrations of 0, 1.4, 7.3, or 22 ppm of the test substance 6 hours per day for a total of 9 exposures.

The atmospheric concentration of the test substance was determined by gas chromatography at approximately 30-minute intervals during exposure. The exposure chambers were also sampled for ammonia and hydrogen cyanide. These compounds are breakdown products of the test substance. Airflow, temperature, and relative humidity were monitored continually.

During the exposure and a 14-day recovery phase rats were weighed and observed each day for clinical signs of toxicity.

After the last exposure, blood and urine samples were collected for clinical analyses, and 5 rats per group were sacrificed for pathologic examination. At the end of the 14-day recovery period, blood and urine samples were again collected, and all surviving rats were sacrificed for pathologic examination. Fifteen hematologic and 17 clinical chemistry parameters were measured or calculated, and 10 urine parameters were measured or examined.

Five rats per group were necropsied on test day 12. After a 14-day recovery period, the remaining 5 rats from each group were similarly necropsied. During the necropsy, liver, kidneys, lungs, testes, and brain were weighed. All rats were given a complete gross examination and representative samples of approximately 38 tissues were saved for possible histopathological evaluation. All tissues from test day 12 rats in the control and high (0 and 22 ppm, respectively) concentration groups were examined microscopically. Liver, kidneys, lungs, larynx/pharynx, nose, testes, and gross lesions from test day 12 low and intermediate (1.4 and 7.3 ppm, respectively) concentration groups, and 14-day recovery control and 22 ppm concentration groups were examined microscopically.

Descriptive statistics were used to summarize experimental data. Mean body weights and body weight gains were statistically analyzed with a one-way analysis of variance (ANOVA). Pairwise comparisons between test and control groups (sexes separate) were made with the Dunnett's test. For clinical laboratory data, ANOVA and Bartlett's test were calculated for each sampling time. Dunnett's test was used to compare means from the control groups and each of the groups exposed to the test substance. When the results of the Bartlett's test were significant, the Kruskal-Wallis test was employed and the Mann-Whitney U test was used to compare means from the control groups and each of the groups exposed to the test substance. Mean final body weights and mean absolute and relative (to body and brain) organ weights were analyzed by ANOVA. When the value of the F-statistic for differences among groups was significant, pairwise comparisons between treated and control groups were made with Dunnett's test. Bartlett's test was used to test for homogeneity of variances.

GLP: Yes

Test Substance: 2-Amino-2-methylpropanenitrile, purity 73-75%

Results: Analytically determined mean vapor concentrations of the test substance for the 3 test chambers were 1.4, 7.3, and 22 ppm. No hydrogen cyanide was found in the 1.4 ppm or 7.3 ppm chambers, but approximately 0.9 ppm was found in the 22 ppm chamber. Low concentrations of ammonia were present in all test chambers (1.5-6 ppm). Concentrations of breakdown products found in the chambers were not considered toxicologically significant.

The mean relative humidity for the chambers was between 37 and 41%, the mean chamber temperatures were 25 or 26°C, and the oxygen concentrations were 21%.

No deaths were observed during the study. No differences in body weight or clinical observations were observed during the study. No toxicologically important changes occurred in hematology, clinical chemistry, or urine analytical parameters. No test substance-related changes in organ weights, gross observation, or microscopic observations were observed at any exposure level tested.

Under the conditions of this study, the no-observed-effect level (NOEL) was 22 ppm.

Reference: DuPont Co. (1998). Unpublished Data, Haskell Laboratory Report No. 1998-01568, "Two-Week Inhalation Toxicity Study in Male Rats" (August 28).

Reliability: Medium because there was no demonstrated effect at the highest concentration tested.

Additional References for Repeated Dose Toxicity: None Found.

5.3 Developmental Toxicity: No Data.

5.4 Reproductive Toxicity: No Data.

5.5 Genetic Toxicity

Type: ***In vitro* Bacterial Reverse Mutation Assay:** No Data.

Type: ***In vitro* Clastogenicity Studies:** No Data.

Type: ***In vivo* Genetic Toxicity Studies:** No Data.

Appendix B

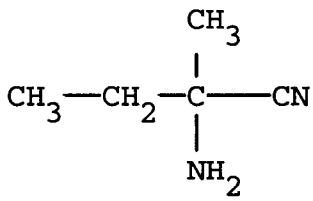
Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as related references at the end of each appropriate section, with a statement to reflect the reason why these studies were not summarized.

1.0 Substance Information

CAS Number: 4475-95-0

Chemical Name: Butanenitrile, 2-amino-2-methyl-

Structural Formula:



Other Names:
1-Cyano-1-methylpropylamine
2-Amino-2-methylbutanenitrile
2-Amino-2-methylbutyronitrile
Isovalinonitrile
Vazo 67 aminonitrile

Exposure Limits: No Data

2.0 Physical/Chemical Properties

2.1 Melting Point/Freezing Point

Value:	7.14
Decomposition:	No Data
Sublimation:	No Data
Pressure:	760 mm Hg
Method:	Modeled. MPBPWIN, v.1.41, module of EPIWIN 3.11 (Syracuse Research Corporation). MPBPWIN estimates melting point by 2 different methods. The first is an adaptation of the Joback group contribution method for melting point (Joback, 1982; Reid et al; 1987) and the second is a simple Gold and Ogle method suggested by Lyman (1985).
GLP:	Not Applicable
Reference:	Joback, K. G. (1982). A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques, Stevens Institute of Technology, submitted to

the Dept. of Chem. Eng. for M.S. Degree at the Massachusetts Institute of Technology in June 1984 (see also: Reid et al., 1987).

Reid, R. C. et al. (1987). The Properties of Gases and Liquids, 4th edition, Chapter 2, McGraw-Hill, Inc., NY.

Lyman, W. J. (1985). In: Environmental Exposure From Chemicals, Volume I, Chapter 2, Neely, W. B. and G. E. Blau (eds.), CRC Press, Inc., Boca Raton, FL.

Reliability: Estimated value based on accepted model.

Additional Reference for Melting Point:

DuPont Co. (2003). Material Safety Data Sheet DU001250 (December 19).

2.2 Boiling Point

Value:	No Data
Decomposition:	Yes
Pressure:	No Data
Method:	No Data
GLP:	Unknown
Reference:	DuPont Co. (2003). Material Safety Data Sheet DU001250 (December 19).
Reliability:	Not assignable because limited study information was available.

Additional References for Boiling Point: None Found.

2.3 Density

Value:	0.886 (Vapor density >1, where air = 1)
Temperature:	No Data
Method:	No Data
GLP:	Unknown
Results:	No additional data.
Reference:	DuPont Co. (2003). Material Safety Data Sheet DU001250 (December 19).
Reliability:	Not assignable because limited study information was available.

Additional References for Density: None Found.

2.4 Vapor Pressure

Value:	14 mm Hg
Temperature:	68°C
Decomposition:	No Data
Method:	No Data
GLP:	Unknown
Reference:	DuPont Co. (2003). Material Safety Data Sheet DU001250 (December 19).
Reliability:	Not assignable because limited study information was available.

Value:	1.03
Temperature:	25°C
Decomposition:	No Data
Method:	Estimated as the mean of Antoine & Grain methods
GLP:	Not Applicable
Reference:	SRC MPBPWIN v1.40 in EPIWIN v3.11. Syracuse Research Corporation (MPBPWIN) program estimates the vapor pressure using the modified Grain method. A description of the methodology is detailed in: Lyman, W. J. (1985). In: Environmental Exposure From Chemicals, Volume I, Chapter 2, Neely, W. B. and G. E. Blau (eds.), CRC Press, Inc., Boca Raton, FL.
Reliability:	Estimated value based on accepted model.

Additional References for Vapor Pressure: None Found.

2.5 Partition Coefficient (log Kow)

Value:	0.45 (SMILES: C(#N)C(N)(C)CC) -2.73 (SMILES: C(#N)C(N(H)(H)(H)(CL))(C)CC) as ionized salt at environmental pH and high dilution
Temperature:	25°C
Method:	Modeled. KOWWIN, v. 1.67, module of EPIWIN 3.11 (Syracuse Research Corporation). KOWWIN uses "fragment constant" methodologies to predict log P. In a "fragment constant" method, a structure is divided into fragments (atom or larger functional groups) and coefficient values of each fragment or group are summed together to yield the log P estimate.
GLP:	Not Applicable
Reference:	Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci., 84:83-92.

Reliability: Estimated value based on accepted model.

Additional References for Partition Coefficient (log Kow): None Found.

2.6 Water Solubility

Value:	27.0 g/L
Temperature:	No Data
pH/pKa:	pKa = 4.9
Method:	Modeled.
	Solubility - WSKOWWIN v.1.41, module of EPIWIN 3.11 (Syracuse Research Corporation). Water solubility is estimated from log Kow using molecular weight and molecular fragment correction factors.
	pKa – SPARC On-line calculator, University of Georgia
GLP:	Not Applicable
Reference:	Solubility - Meylan, W. M. et al. (1996). Environ. Toxicol. Chem., 15:100-106.
	pKa - http://ibmlc2.chem.uga.edu/sparc/index.cfm
Reliability:	Estimated value based on accepted model.

Additional Reference for Water Solubility:

DuPont Co. (2003). Material Safety Data Sheet DU001250 (December 19).

2.7 Flash Point

Value:	1.7°C (autodecomposition ~80°C)
Method:	SFCC
GLP:	Unknown
Reference:	DuPont Co. (2003). Material Safety Data Sheet DU001250 (December 19).
Reliability:	Not assignable because limited study information was available.

Additional References for Flash Point: None Found.

2.8 Flammability

Results:	Flammable liquid
Method:	No Data
GLP:	Unknown

Reference:	DuPont Co. (2003). Material Safety Data Sheet DU001250 (December 19).
Reliability:	Not assignable because limited study information was available.

Additional References for Flammability: None Found.

3.0 Environmental Fate

3.1 Photodegradation

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	No Data
Indirect Photolysis:	Estimated half-life = 10.8 days, due to OH radical oxidation in the atmosphere. With an estimated vapor pressure of 1.03 mm Hg (25°C) 2-amino-2-methylbutanenitrile will exist as a vapor in the atmosphere.
Breakdown Products:	No Data
Method:	Modeled
GLP:	Not Applicable
Reference:	Indirect Photolysis: AOPWIN, v1.91 module of EPIWIN 3.11. Meylan, W. M. and P. H. Howard (1993). Chemosphere, 26:2293-2299.
Reliability:	Estimated value based on accepted model.

Additional References for Photodegradation: None Found.

3.2 Stability in Water

Concentration:	No Data
Half-life:	In the presence of water and the absence of excess ammonia, aminonitriles may disproportionate into their constituents: ketone, cyanide, and ammonium (Kirk-Othmer, 1978)
% Hydrolyzed:	No Data
Method:	Modeled. HYDROWIN, v. 1.67 module of EPIWIN v3.11 (Syracuse Research Corporation). HYDROWIN cannot estimate a hydrolysis rate constant for this type of chemical structure.
GLP:	Not Applicable
Reference:	Kirk-Othmer Encyclopedia of Chemical Technology (1978). 3rd edition, Wiley-Interscience. Mill, T. et al. (1987). "Environmental Fate and Exposure Studies Development of a PC-SAR for Hydrolysis: Esters, Alkyl Halides and Epoxides," EPA Contract No.

68-02-4254, SRI International, Menlo Park, CA.

Reliability: Estimated value based on accepted model.

Additional References for Stability in Water: None Found.

3.3 Transport (Fugacity)

Media: Air, Water, Soil, and Sediments

Distributions:

Compartment	% of total distribution	½ life (hours) (advection + reaction)
Air	0.1	696
Water	44.8	900
Soil	55	1800
Sediment	0.09	8100

Adsorption Coefficient: Koc = 0.231 (calc by model)

Desorption: No Data

Volatility: Henry's Law Constant = 7.35×10^{-9} atm-m^3/mole (HENRYWIN program)

Method: Modeled.

SMILES: C(#N)C(N)(C)CC
Molecular Wt: 98.15
Vapor Pressure: 1.03 mm Hg (MPBPWIN program)
Log Kow: -0.25 (KOWWIN program)

Henry's Law Constant - HENRYWIN v. 3.10 module of EPIWIN v3.11 (Syracuse Research Corporation). Henry's Law Constant (HLC) is estimated by 2 separate methods that yield two separate estimates. The first method is the bond contribution method and the second is the group contribution method. The bond contribution method is able to estimate many more types of structures; however, the group method estimate is usually preferred (but not always) when all fragment values are available.

Koc – Calculated from log Kow by the Mackay Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation).

Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v3.11 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments.

GLP: Not Applicable

Reference: HENRYWIN –

J. Hine and P. K. Mookerjee (1975). J. Org. Chem., 40(3):292-298.

Meylan, W. and P. H. Howard (1991). Environ. Toxicol. Chem., 10:1283-1293.

Fugacity - The methodology and programming for the Level III fugacity model incorporated into EPIWIN v3.05 (Syracuse Research Corporation) were developed by Dr. Donald MacKay and coworkers and are detailed in:

Mackay, D. (1991). Multimedia Environmental Models: The Fugacity Approach, pp. 67-183, Lewis Publishers, CRC Press.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1618-1626.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1627-1637.

Reliability: Estimated values based on accepted models.

Additional References for Transport (Fugacity):

3.4 Biodegradation

Value:

Linear Model Prediction:	0.9777 (Biodegrades Fast)
Non-Linear Model Prediction:	0.9965 (Biodegrades Fast)
Ultimate Biodegradation Timeframe:	2.7122 (weeks-months)
Primary Biodegradation Timeframe:	3.5308 (days-weeks)
MITI Linear Model Prediction:	0.6429 (readily degradable)

MITI Non-Linear Model Prediction:	0.6249 (readily degradable)
Breakdown Products:	No Data
Method:	Modeled. BIOWIN, v. 4.01 module of EPINWIN v3.11 (Syracuse Research Corporation). BIOWIN estimates the probability for the rapid aerobic biodegradation of an organic chemical in the presence of mixed populations of environmental microorganisms. Estimates are based upon fragment constants that were developed using multiple linear and non-linear regression analyses.
GLP:	Not Applicable
Reference:	Boethling, R. S. et al. (1994). Environ. Sci. Technol., 28:459-65. Howard, P. H. et al. (1992). Environ. Toxicol. Chem., 11:593-603. Howard, P. H. et al. (1987). Environ. Toxicol. Chem., 6:1-10. Tunkel, J. et al. (2000). Predicting Ready Biodegradability in the MITI Test. Environ. Toxicol. Chem., 19(10):2478-2485.
Reliability:	Estimated value based on accepted model.

Additional References for Biodegradation: None Found.

3.5 Bioconcentration

Value:	log BCF = 0.5 (unionized or salt)
Method:	Modeled. BCFWIN v. 2.15 module of EPINWIN v3.11 (Syracuse Research Corporation). BCFWIN estimates the bioconcentration factor (BCF) of an organic compound using the compound's log octanol-water partition coefficient (Kow) with correction factors based on molecular fragments.
GLP:	Not Applicable
Reference:	"Improved Method for Estimating Bioconcentration Factor (BCF) from Octanol-Water Partition Coefficient", SRC TR-97-006 (2nd Update), July 22, 1997; prepared for Robert S. Boethling, EPA-OPPT, Washington, DC, Contract No. 68-D5-0012; prepared by William M. Meylan, Philip H. Howard, Dallas Aronson, Heather Printup, and Sybil Gouchie, Syracuse Research Corp.

Reliability: Estimated value based on accepted model.

Additional References for Bioconcentration: None Found.

4.0 Ecotoxicity

4.1 Acute Toxicity to Fish

Type: **96-Hour LC_{50}**
Species: Fathead minnow, *Pimephales promelas*
Value: 0.71 mg/L
Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

A 96-hour unaerated, static, acute test using fathead minnows was performed at nominal concentrations of 0, 0.5, 1.0, 50, 500, and 5000 mg/L. Dissolved oxygen and pH were measured in the 0, 0.5, 50, and 5000 mg/L nominal concentrations. No information regarding hardness, alkalinity, pH, TOC, TSS, or salinity of the dilution water chemistry was reported.
GLP: No
Test Substance: 2-Amino-2-methylbutanenitrile, purity 78%
Results: Mortalities of 0, 0, 100, 100, 100, and 100% were observed at 0, 0.5, 1.0, 50, 500, and 5000 mg/L, respectively. Based on visual observations, the test substance was soluble in well water at all but the highest test concentration. At 5000 mg/L, a precipitate was seen after 24 hours. The dissolved oxygen at 0 and 96 hours or at total mortality were 8.8, 8.9, 8.7, and 8.8 mg/L and 7.2, 5.8, 8.7, and 8.8, for the 0, 0.5, 1.0, 50, 500, and 5000 mg/L groups, respectively. The pH values at 0 and 96 hours or at total mortality were 6.8, 6.8, 8.6, and 9.5 and 6.9, 6.9, 8.6, and 9.5 for the 0, 0.5, 1.0, 50, 500, and 5000 mg/L groups, respectively.
Reference: DuPont Co. (1992). Unpublished Data, Haskell Laboratory Report No. 790-92, "Static, Acute 96-Hour Screening Test to Fathead Minnows, *Pimephales promelas*" (November 18).
Reliability: Medium because a suboptimal study design (nominal test concentrations) was used.

Type: **96-hour LC_{50}**
Species: Fish
Value: 744.5 mg/L; log Kow = -0.25
Method: Modeled
GLP: Not Applicable
Test Substance: 2-Amino-2-methyl butanenitrile

Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Fish: None Found.

4.2 Acute Toxicity to Invertebrates

Type:	**48-hour LC_{50}**
Species:	*Daphnia*
Value:	41.1 mg/L; log Kow = -0.25
Method:	Modeled
GLP:	Not Applicable
Test Substance:	2-Amino-2-methyl butanenitrile
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Invertebrates: None Found.

4.3 Acute Toxicity to Aquatic Plants

Type:	**96-hour EC_{50}**
Species:	Fish
Value:	35.7 mg/L; log Kow = -0.25
Method:	Modeled
GLP:	Not Applicable
Test Substance:	2-Amino-2-methyl butanenitrile
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by

	Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Aquatic Plants: None Found.

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type:	**Oral LD_{50}**
Species/Strain:	Male rats/ChR-CD
Value:	74 mg/kg (95% confidence limits, 71-76 mg/kg)
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. The test substance, as a suspension in corn oil, was administered by gavage in single doses to 4 groups of 10 young adult rats. Dose levels were 70, 75, 80, and 90 mg/kg. The surviving rats were weighed and observed during a 14-day recovery period, and then sacrificed. The LD_{50} value was calculated from the mortality data using the method of D. J. Finney.
GLP:	No
Test Substance:	2-Amino-2-methylbutanenitrile, purity 80%
Results:	Mortality was 1/10, 7/10, 9/10, and 10/10 at 70, 75, 80, and 90 mg/kg, respectively. All deaths occurred within 1 day after dosing. At 70 mg/kg only slight initial weight loss was observed. At 75 mg/kg, lethargy, gasping, moribundity, and prostration were observed on the day of dosing. Slight weight loss was observed in 2 of the 3 survivors on the day after dosing. At 80 mg/kg, salivation, tremors, lethargy, moribundity, prostration, and weakness were observed on the day of dosing. Slight weight loss was observed in the 1 survivor on the day after dosing. At 90 mg/kg, tremors, convulsions, gasping, lethargy, and moribundity were observed on the day of dosing.
Reference:	DuPont Co. (1980). Unpublished Data, Haskell Laboratory Report No. 498-80, "Oral LD_{50} Test in Rats" (June 12) (also cited in TSCA Fiche OTS0555327).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Acute Oral Toxicity: None Found.

Type:	**Inhalation LC_{50}**
Species/Strain:	Male and female rats/Crl:CD®BR
Exposure Time:	1 hour
Value:	107 ppm (estimated for male and female rats combined)
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Groups of 5 male and 5 female rats were exposed for 1 hour to the test substance in air at mean vapor concentrations of 102, 106, 120, 126, and 225 ppm. Rats were exposed nose-only. Rats were weighed prior to exposure, and were observed for clinical signs of toxicity during exposure. Surviving rats were weighed and observed daily for 14 days. No pathological evaluations were performed. Two analytical methods were used to measure the atmospheric concentration of the test substance. A gas chromatographic analysis was used to measure the atmospheric concentration of aminonitrile vapor (active ingredient). A colorimetric method was used to estimate the atmospheric concentration of ammonia. Chamber temperature, relative humidity, and chamber oxygen content were recorded.
GLP:	Yes
Test Substance:	2-Amino-2-methylbutanenitrile, purity 74.9%
Results:	Chamber temperature ranged from 28-34°C, relative humidity ranged from 9-19%, and chamber oxygen content was 21%. Mortality in male rats was 0/5, 3/5, 5/5, 3/5, and 5/5 at 102, 106, 120, 126, and 225 ppm, respectively. Mortality in female rats was 0/5, 5/5, 5/5, 5/5, and 5/5 at 102, 106, 120, 126, and 225 ppm, respectively. The majority of the deaths occurred during exposure, with remaining deaths occurring within 1 day of exposure. During exposure, rats in all groups had a red nasal discharge and a diminished response to sound. Rats that survived the exposure were lethargic or prostrate when released from the restrainers. Rats that survived the recovery period had no significant weight loss or adverse clinical signs. The LC_{50} for male rats was 111 ppm. The LC_{50}'s for female rats and for both sexes combined could not be calculated due to the steep dose-response observed. However, these LC_{50}'s were estimated to be 104 and 107 ppm, respectively.

	Estimated ammonia concentrations were well below those expected to cause death.
Reference:	DuPont Co. (1987). Unpublished Data, Haskell Laboratory Report No. 324-87, "One-Hour Inhalation Median Lethal Concentration (LC_{50}) Study in Rats" (August 24) (also cited in TSCA Fiche OTS0546376).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Acute Inhalation Toxicity: None Found.

Type:	**Dermal Toxicity:** No Data.

Type:	**Dermal Irritation**
Species/Strain:	Male rabbits/New Zealand White
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study. Six rabbits were clipped free of hair on the trunk and lateral area, and placed in FDA-type stocks. Doses of 0.5 mL of the test substance were applied to intact skin under gauze squares. Rubber sheeting was then loosely wrapped around the trunk and secured with adhesive tape. After 24 hours, the rabbits were removed from the stocks, the patches taken off, and the reactions observed. Observations were also made at 48 hours.
GLP:	No
Test Substance:	2-Amino-2-methylbutanenitrile, purity 80%
Results:	At the 24-hour observation, slight erythema in 3/6 rabbits and no erythema in 3/6 rabbits was observed. At the 48-hour observation, slight erythema in 2/6 rabbits and no erythema in 4/6 rabbits was observed. No edema was observed throughout the study.
Reference:	DuPont Co. (1980). Unpublished Data, Haskell Laboratory Report No. 512-80, "Skin Irritation Test on Rabbits" (June 17).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional Reference for Dermal Irritation:

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1980). Unpublished Data, Haskell Laboratory Report No. 510-80, "Primary Skin Irritation and Sensitization Test on Guinea Pigs" (June 17).

Type:	**Dermal Sensitization**
Species/Strain:	Male guinea pigs/Duncan Hartley
Method:	No specific test guideline was reported; however, the design is a modification of the Buehler method. The primary irritation test was conducted on 10 unexposed guinea pigs with 0.05 mL of a 100% (as received) solution and 10% solution of the test substance in dimethyl phthalate (DMP) on shaved intact shoulder skin. The induction phase for sensitization was a series of 4 sacral intradermal injections of 0.1 mL of a 1.0% solution in DMP, 1 each week beginning 2 days after the test for primary irritation. After a 13-day rest period, the test guinea pigs were challenged for sensitization with 0.05 mL of a 100% (as received) solution and a 10% solution of test substance in DMP on shaved, intact shoulder skin. At the same time 10 unexposed guinea pigs (controls) of the same age received identical topical applications.
GLP:	No
Test Substance:	2-Amino-2-methylbutanenitrile, purity 80%
Results:	The test substance produced neither sensitization nor irritation in 10 male guinea pigs.
Reference:	DuPont Co. (1980). Unpublished Data, Haskell Laboratory Report No. 510-80, "Primary Skin Irritation and Sensitization Test on Guinea Pigs" (June 17).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Dermal Sensitization: None Found.

Type:	**Eye Irritation**
Species/Strain:	Male rabbits/Albino
Method:	One-tenth mL of undiluted test substance was placed into the right conjunctival sac of each of 2 rabbits. After 20 seconds, 1 treated eye was washed with tap water for 1 minute. The treated eye of the other rabbit was not washed. Observations of the cornea, iris, and conjunctiva were made with a hand-slit lamp at 1 and 4 hours, and at 1, 2, 3, 14, 21, 27, and 34 days. Fluor-i-strip® stain and a biomicroscope were used at examinations after the day of treatment.
GLP:	No
Test Substance:	2-Amino-2-methylbutanenitrile, purity 80%
Results:	The test substance produced generalized moderate to severe

	corneal cloudiness with the development of pannus, moderate iritis, and severe conjunctivitis. Severe generalized cloudiness and moderate iritis persisted. The conjunctiva was normal at 27 days. An eye dosed with the test substance and promptly washed had a small area of transient slight corneal cloudiness and mild conjunctivitis with no iritic effects. The washed eye was normal at 2 days.
Reference:	DuPont Co. (1980). Unpublished Data, Haskell Laboratory Report No. 558-80, "Eye Irritation Test in Rabbits" (August 11).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Eye Irritation: None Found.

5.2 Repeated Dose Toxicity: Not Required.

5.3 Developmental Toxicity: No Data.

5.4 Reproductive Toxicity: Not Required.

5.5 Genetic Toxicity

Type:	***In vitro* Bacterial Reverse Mutation Assay:** No Data.
Type:	***In vitro* Clastogenicity Studies:** No Data.
Type:	***In vivo* Genetic Toxicity:** No Data.

Appendix C

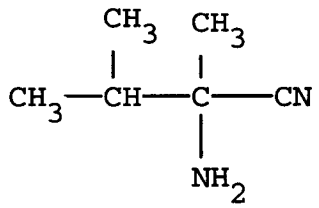
Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as related references at the end of each appropriate section, with a statement to reflect the reason why these studies were not summarized.

1.0 Substance Information

CAS Number: 13893-53-3

Chemical Name: 2-Amino-2,3-dimethylbutanenitrile

Structural Formula:



Other Names: Aminonitrile

Exposure Limits: 4.7 ppm (5 mg/m^3): PEL/TLV

2.0 Physical/Chemical Properties

2.1 Melting Point

Value:	7.67°C
Decomposition:	No Data
Sublimation:	No Data
Pressure:	760 mm Hg
Method:	Modeled. MPBPWIN, v.1.41, module of EPIWIN 3.11 (Syracuse Research Corporation). MPBPWIN estimates melting point by 2 different methods. The first is an adaptation of the Joback group contribution method for melting point (Joback, 1982; Reid et al; 1987) and the second is a simple Gold and Ogle method suggested by Lyman (1985).
GLP:	Not Applicable
Reference:	Joback, K. G. (1982). A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques, Stevens Institute of Technology, submitted to the Dept. of Chem. Eng. for M.S. Degree at the Massachusetts Institute of Technology in June 1984 (see also: Reid et al., 1987).

Reid, R. C. et al. (1987). The Properties of Gases and Liquids, 4th edition, Chapter 2, McGraw-Hill, Inc., NY.

Lyman, W. J. (1985). In: Environmental Exposure From Chemicals, Volume I, Chapter 2, Neely, W. B. and G. E. Blau (eds.), CRC Press, Inc., Boca Raton, FL.

Reliability: Estimated value based on accepted model.

Additional Reference for Melting Point:

Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).

2.2 Boiling Point

Value:	186.88°C
Decomposition:	Yes
Pressure:	No Data
Method:	Estimated by the MPBPWIN Program (v. 1.40), using the adapted Stein and Brown Method.
GLP:	Not Applicable
Reference:	Syracuse Research Corporation, Syracuse, NY
	Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998 (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).
Reliability:	Klimisch code: 2f

Additional References for Boiling Point: None Found.

2.3 Density: No Data.

2.4 Vapor Pressure

Value:	0.6 mm Hg
Temperature:	25°C
Decomposition:	No Data
Method:	Estimated by the MPBPWIN Program (v. 1.40), using mean of Antoine and Grain methods.
GLP:	Not Applicable

Reference:	Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998 (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).
Reliability:	Klimisch code: 2f

Value:	23.42 mm Hg
Temperature:	25°C
Decomposition:	No Data
Method:	The vapor pressure was measured using a static method. The sample was placed in a glass cell and degassed using five freeze-pump-thaw cycles. The sample temperature was measured to ±0.01°C with a Hewlett-Packard Quartz Thermometer and controlled to ±1°C with a Blue-M forced air oven. The pressure was measured with a MKS Baratron capacitance transducer. The sample was stable during the experiment with no discoloration and it gave stable pressure reading once thermal equilibration was achieved.
GLP:	No
Reference:	American Cyanamid Company (1988). Stamford Research Center (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).
Reliability:	Klimisch code: 2e. This study was not conducted under GLP or OECD guidelines, but generally meets scientific standards, is well documented, and is accepted for assessment.

Additional References for Vapor Pressure: None Found.

2.5 Partition Coefficient (log Kow)

Value:	0.87 (SMILES: C(#N)C(N)(C(C)C)C) -2.32 (SMILES: C(#N)C(N(H)(H)(H)(CL))(C(C)C)C) as ionized salt at acidic environmental pH and high dilution
Temperature:	No Data

Method:	Modeled. KOWWIN, v.1.67, module of EPIWIN 3.11 (Syracuse Research Corporation). KOWWIN uses "fragment constant" methodologies to predict log P. In a "fragment constant" method, a structure is divided into fragments (atom or larger functional groups) and coefficient values of each fragment or group are summed together to yield the log P estimate.
GLP:	Not Applicable
Reference:	Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci., 84:83-92.
Reliability:	Estimated value based on accepted model.

Additional References for Partition Coefficient (log Kow): None Found.

2.6 Water Solubility

Value:	1.07 E+5 mg/L
Temperature:	25°C
pH/pKa:	pKa = 4.9
Method:	Estimated from Kow with WSKOW (v1.40): KowWin Estimate
GLP:	Not Applicable
Reference:	Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998 (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003). pKa - http://ibmlc2.chem.uga.edu/sparc/index.cfm
Reliability:	Klimisch code: 2f

Additional References for Water Solubility: None Found.

2.7 Flash Point: No Data.

2.8 Flammability: No Data.

3.0 Environmental Fate

3.1 Photodegradation

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	No Data
Indirect Photolysis:	For reaction with hydroxyl radicals, the predicted half-life of the chemical is relatively rapid. Rate constant: 2.888×10^{-12} cm3/molecule-sec Half-life: 44.443 hours
Breakdown Products:	No Data
Method:	Estimated by the AOP program (v1.90), which estimates rate constants and half-lives of atmospheric reactions of organic compounds with hydroxyl radicals and ozone in the atmosphere.
GLP:	Not Applicable
Reference:	Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998 (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).
Reliability:	Klimisch code: 2f

Additional References for Photodegradation: None Found.

3.2 Stability in Water

Concentration:	No Data
Half-life:	No estimate available
% Hydrolyzed:	The program was not able to estimate a hydrolysis rate constant for this type of chemical structure. However, as manufactured, 2-amino-2,3-dimethylbutanenitrile is prepared as an 80% solution in toluene, and this solution will partially hydrolyze in water by producing CN^-, which will be detectable immediately. A small fraction of the 2-amino-2,3-dimethylbutanenitrile dissociates under ambient conditions, whether as neat (100%) liquid or in solution with non-reactive organic solvents such as toluene. CN^- is a

product of the dissociation of 2-amino-2,3-dimethylbutanenitrile and will be present in a low concentration in equilibrium with 2-amino-2,3-dimethylbutanenitrile under all expected conditions.

Aqueous wastes containing 2-amino-2,3-dimethylbutanenitrile, when commingled with a waste stream that is maintained at a pH of at least 10 by the addition of caustic, chemically decomposes the 2-amino-2,3-dimethylbutanenitrile to CN^-, ammonia, and methyl isopropyl ketone. Thus indicating that with pH increase the material decomposes.

Method: Estimated by the HYDROWIN program (v.1.67)
GLP: Not Applicable
Reference: Syracuse Research Corporation, Syracuse, NY

Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998 (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).
Reliability: Estimated data based on accepted model.

Additional References for Stability in Water: None Found.

3.3 Transport (Fugacity)

Media: Air, Water, Soil, and Sediments
Distributions:

Compartment	% of total distribution	½ life (hours) (advection + reaction)
Air	0.127	133
Water	42.2	900
Soil	57.6	1800
Sediment	0.087	8100

Adsorption Coefficient: Koc = 3.04 (calc by model)
Desorption: No Data
Volatility: Henry's Law Constant = 9.76×10^{-9} atm-m^3/mole (HENRYWIN program)
Method: Modeled.

Henry's Law Constant - HENRYWIN v. 3.10 module of

EPIWIN v3.11 (Syracuse Research Corporation). Henry's Law Constant (HLC) is estimated by two separate methods that yield two separate estimates. The first method is the bond contribution method and the second is the group contribution method. The bond contribution method is able to estimate many more types of structures; however, the group method estimate is usually preferred (but not always) when all fragment values are available.

Koc – Calculated from Kow by the Mackay Level III fugacity model incorporated into EPIWIN v3.11 (Syracuse Research Corporation).

Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v3.11 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments.

GLP: Not Applicable

Reference: HENRYWIN –

J. Hine and P. K. Mookerjee (1975). J. Org. Chem., 40(3):292-298.

Meylan, W. and P. H. Howard (1991). Environ. Toxicol. Chem., 10:1283-1293.

Fugacity - The methodology and programming for the Level III fugacity model incorporated into EPIWIN v3.05 (Syracuse Research Corporation) were developed by Dr. Donald MacKay and coworkers and are detailed in:

Mackay, D. (1991). Multimedia Environmental Models: The Fugacity Approach, pp. 67-183, Lewis Publishers, CRC Press.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1618-1626.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1627-1637.

Reliability: Estimated values based on accepted models.

Additional Reference for Transport (Fugacity):

Data from this additional source supports the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998 (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).

Biodegradation

Value:	
Linear Model Prediction:	0.9710 (Biodegrades Fast)
Non-Linear Model Prediction:	0.9957 (Biodegrades Fast)
Ultimate Biodegradation Timeframe:	2.6812 (weeks-months)
Primary Biodegradation Timeframe:	3.5105 (days-weeks)
MITI Linear Model Prediction:	0.5015 (readily degradable)
MITI Non-Linear Model Prediction:	0.3999 (not readily degradable)
Breakdown Products:	No Data
Method:	Modeled. BIOWIN, v. 4.01 module of EPINWIN v3.11 (Syracuse Research Corporation). BIOWIN estimates the probability for the rapid aerobic biodegradation of an organic chemical in the presence of mixed populations of environmental microorganisms. Estimates are based upon fragment constants that were developed using multiple linear and non-linear regression analyses.
GLP:	Not Applicable
Reference:	Boethling, R. S. et al. (1994). Environ. Sci. Technol., 28:459-65. Howard, P. H. et al. (1992). Environ. Toxicol. Chem., 11:593-603. Howard, P. H. et al. (1987). Environ. Toxicol. Chem., 6:1-10.

	Tunkel, J. et al. (2000). Predicting Ready Biodegradability in the MITI Test. Environ. Toxicol. Chem., 19(10):2478-2485.
Reliability:	Estimated value based on accepted model.

Additional Reference for Biodegradation:

Data from this additional source supports the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

Syracuse Research Corporation (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).

3.4 Bioconcentration:

Value:	log BCF = 0.5 (unionized or salt)
Method:	Modeled. BCFWIN v. 2.15 module of EPINWIN v3.11 (Syracuse Research Corporation). BCFWIN estimates the bioconcentration factor (BCF) of an organic compound using the compound's log octanol-water partition coefficient (Kow) with correction factors based on molecular fragments.
GLP:	Not Applicable
Reference:	"Improved Method for Estimating Bioconcentration Factor (BCF) from Octanol-Water Partition Coefficient", SRC TR-97-006 (2nd Update), July 22, 1997; prepared for Robert S. Boethling, EPA-OPPT, Washington, DC, Contract No. 68-D5-0012; prepared by William M. Meylan, Philip H. Howard, Dallas Aronson, Heather Printup, and Sybil Gouchie, Syracuse Research Corp.
Reliability:	Estimated value based on accepted model.

Additional References for Bioconcentration: None Found.

4.0 Ecotoxicity

4.1 Acute Toxicity to Fish

Type:	**96-hour LC_{50}**
Species:	*Lepomis macrochirus* (bluegill sunfish)
Value:	0.75 mg/L
Method:	Patterned after EPA-660-3-75-009. ABC Laboratories Protocol 7601 (American Cyanamid Protocol 981-83-140).

The static fish bioassay was conducted in 5-gallon glass vessels containing 15 liters of soft reconstituted water. Ten fish with a mean weight of 0.34 g and a mean length of 25 mm were used for each test concentration. The test vessels were kept in a water bath at 22±1°C. A 48-hour range-finding test was conducted to determine the concentration range for the definitive study. The preliminary test concentrations were set at 0.1, 1.0, and 10 mg/L. Based on the results of the preliminary testing, 5 test concentrations were selected, 0.10, 0.18, 0.32, 0.56, and 1.0 mg/L. Exposures were based on nominal concentrations. Test concentrations were prepared by preparing a stock solution in deionized water and serially diluting to obtain desired concentrations. All results were based on the nominal concentrations.

The bluegill sunfish were challenged with a reference compound, Antimycin A, to verify that the fish were in good condition. The 96-hour LC_{50} for bluegill sunfish exposed to the control substance was 1.2×10^{-4} mg/L, which indicates that the fish were in good condition.

The fish were observed once every 24 hours for mortality and abnormal effects. Water quality parameters of temperature, dissolved oxygen, and pH were measured throughout the test and were within acceptable limits.

Statistical analysis of the concentration versus effect data was obtained by employing a computerized LC_{50} program developed by Stephan. This program calculated the LC_{50} statistic and its 95% confidence limits using the binomial and the moving average tests, respectively. The method of calculation selected for use was that which gave the narrowest confidence limits for the LC_{50}.

GLP: The study was conducted following the intent of Good Laboratory Practices.

Test Substance: 2-Amino-2,3-dimethylbutanenitrile, purity not reported

Results: The no-effect concentration for the test material, based on the lack of mortality and abnormal effects was estimated to be 0.5 mg/L after 96 hours. All the fish in the 1.0 mg/L test concentration died on or before the 24-hour observation period. Water quality parameters of temperature, dissolved oxygen, and pH were measured throughout the test and were within acceptable limits.

Reference: American Cyanamid Company (1984). ABC Laboratories Report # 31250 (cited in Cytec Industries, Inc. (2001). High

	Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).
Reliability:	Klimisch code: 2c

Type:	**96-hour LC_{50}**
Species:	Fish
Value:	163.3 mg/L; log Kow = 0.87
Method:	Modeled
GLP:	Not Applicable
Test Substance:	2-Amino-2,3-dimethyl butanenitrile
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Fish: None Found.

4.2 Acute Toxicity to Invertebrates

Type:	**48-hour EC_{50}**
Species:	*Daphnia magna*
Value:	6.9 mg/L
Method:	Based on methods outlined in the Committee on Methods for Toxicity Test with Aquatic Organisms, USEPA 600/3-75009. ABC Laboratories Protocol 7806 (American Cyanamid Protocol 981-83-137). The static *Daphnia magna* bioassay was conducted in 250 mL glass beakers, 10 daphnids/beaker, containing 200 mL of ABC well water. These vessels were kept at 20±2°C. The lighting was maintained at 50-70 foot-candles on a 16-hour daylight photoperiod. An initial range-finding test was conducted to determine the concentration range for the definitive study. The preliminary test concentrations were set at 0.1, 1.0, and 10 mg/L. Based on the results of the preliminary testing, 5 test concentrations were selected and tested in duplicate, 0 (control), 0.56, 1.0, 1.8, 3.2, 5.6, and 10 mg/L.

	Test concentrations were prepared by preparing a stock solution in deionized water and serially diluting to obtain desired concentrations. All results were based on the nominal concentrations. Water quality parameters of temperature, dissolved oxygen, and pH were measured at the termination of the test and were within acceptable limits. Statistical analysis of the concentration versus effect data was obtained by employing a computerized LC_{50} program developed by Stephan. This program calculated the LC_{50} statistic and its 95% confidence limits using the binomial and moving average tests. The method of calculation selected for use was that which gave the narrowest confidence limits for the LC_{50}.
GLP:	The study was conducted following the intent of the Good Laboratory Practice Regulations.
Test Substance:	2-Amino-2,3-dimethylbutanenitrile, purity not reported
Results:	Water quality parameters of temperature, dissolved oxygen, and pH were measured at the termination of the test and were within acceptable limits. The dissolved oxygen concentrations, which ranged between 8.4 and 8.8 mg/L, were considered adequate for testing. The pH values of the treated chambers were consistent with the control and ranged from 8.2 to 8.7. The no-effect concentration based on the lack of mortality and abnormal effects was 3.2 mg/L. The abnormal effects of mortality and/or daphnids lying on the bottom were observed after 24 and 48 hours of exposure in the 5.6 mg/L (24-hour: 2/20 dead; 48-hour: 3/20 dead) and 10 mg/L (24-hour: 15/20 dead; 48-hour: 20/20 dead) test concentrations.
Reference:	American Cyanamid Company (1984). ABC Laboratories Report # 31251 (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).
Reliability:	Klimisch code: 2c
Type:	**48-hour LC_{50}**
Species:	*Daphnia*
Value:	10.4 mg/L; log Kow = 0.87
Method:	Modeled
GLP:	Not Applicable
Test Substance:	2-Amino-2,3-dimethyl butanenitrile

Results: No additional data.

Reference: Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.

Reliability: Estimated value based on accepted model.

Additional References for Acute Toxicity to Invertebrates: None Found.

4.3 Acute Toxicity to Aquatic Plants

Type: **96-hour EC_{50}**

Species: *Selenastrum capricornutum*

Value: 0.36 mg/L (confidence limits, 0.24-0.52 mg/L)

Method: Patterned after EPA 600/9-78-016/OTS/ASTM. ABC Laboratories Protocol 8004.

Temperature and light readings were measured throughout the test and were within acceptable limits. The static algal toxicity study was conducted in 250 mL Erlenmeyer flasks containing 100 mL of synthetic algal nutrient medium. This media was composed of 1.0 mL of a salt solution diluted to a final volume of 1000 mL of deionized water. The deionized water was filtered through a Millipore Milli-Q water purification system. After the media was prepared, the pH was adjusted to 7.5 and filter-sterilized through a 0.45 µm filter. To each flask was added 1 mL of algal inoculum containing $2x10^6$±10% cells. The test vessels were incubated for 96 hours at 24±2°C under continuous "cool white" fluorescent light and constant shaking. Temperature and light intensity were monitored throughout the study. Log phase growth was confirmed at 96-hours with a count of $6.9x10^5$ cells/mL in the control. A 96-hour range finding study was conducted to determine the concentration range for the definitive study. Based on the results of the range-finder, test concentrations were set at 0, 0.01, 0.1, 0.5, 1.0, and 10 mg/L. Test flasks were prepared in triplicate for each test concentration and the control. Test concentrations were prepared by preparing a stock solution in deionized water and serially diluting to obtain desired concentrations. Statistical analysis of the concentration versus effect data was obtained by employing a computerized LC_{50} program developed by Stephan. This program calculated the LC_{50}

	statistic and its 95% confidence limits using the moving average test. The method of calculation selected for use was that which gave the narrowest confidence limits for the LC_{50}. The no effect level was determined by using ANOVA and a multiple means comparison test (Fisher's LSD).
GLP:	The study was conducted following the intent of Good Laboratory Practices.
Test Substance:	2-Amino-2,3-dimethylbutanenitrile, purity not reported
Results:	Gravimetric determinations of algal growth at each test concentration (0, 0.01, 0.1, 0.5, 1.0, and 10 mg/L) indicated percent effected as 7, 7, 7, 58, 95, and 100, respective to the concentrations tested. The no-effect level for the test compound was 0.10 mg/L.
Reference:	American Cyanamid Company (1984). ABC Laboratories Report # 31252 (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).
Reliability:	Klimisch code: 2c

Type:	**96-hour EC_{50}**
Species:	Algae
Value:	13.3 mg/L; log Kow = 0.87
Method:	Modeled
GLP:	Not Applicable
Test Substance:	2-Amino-2,3-dimethyl butanenitrile
Results:	No additional data.
Reference:	Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210.
Reliability:	Estimated value based on accepted model.

Additional References for Acute Toxicity to Aquatic Plants: None Found.

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type:	**Oral LD_{50}**
Species/Strain:	Male rat/Sprague-Dawley
Value:	83 mg/kg bw

Method:	Animals were housed at room temperature, 5/cage, and were fasted 18 hour before dosing. Test material was suspended in corn oil. Ten male rats received neat 2-amino-2,3-dimethylbutanenitrile by gavage in corn oil (5% w/v) at concentrations of 31.3, 62.5, and 125 mg/kg. Animals were dosed by oral gavage and observed several times after dosing, and twice daily over a 14-day period for physical condition and mortality.
GLP:	No
Test Substance:	2-Amino-2,3-dimethylbutanenitrile, purity >95%
Results:	Toxic signs seen in all 10 animals at the highest dose and in 1 animal at the intermediate dose included tremors, tonic convulsions, salivation, and prostration. All animals in the 125 mg/kg dose group and 1 of the rats in the 62.5 mg/kg dose group died within 8 hours of dosing.
Reference:	American Cyanamid Company (1983). Acute Oral Toxicity of CL 94,149 (March 4) (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003). American Cyanamid Company (1988). TSCA Fiche OTS0516617.
Reliability:	Klimisch code: 2e. This study was not conducted under GLP or OECD guidelines, but generally meets scientific standards, is well documented, and is accepted for assessment.

Additional References for Acute Oral Toxicity: None Found.

Type:	**Inhalation LC_{50}**
Species/Strain:	Male and female rats/Sprague-Dawley
Exposure Time:	4 hours
Value:	73 ppm (confidence limits, 67-79 ppm)
Method:	OECD Guideline 403 "Acute Inhalation Toxicity" Each group, containing 5 male and 5 female rats, was exposed once for 4 hours to vapor dynamically generated from 2-amino-2,3-dimethylbutanenitrile. The chamber atmosphere was monitored for 2-amino-2,3-dimethylbutanenitrile and hydrogen cyanide. Body weight gains were observed for all survivors on days 7 and 14. Clinical signs and macroscopic findings were recorded.

GLP:	Yes
Test Substance:	2-Amino-2,3-dimethylbutanenitrile, 96% in toluene
Results:	The mean concentrations of 2-amino-2,3-dimethylbutanenitirle and (HCN) for the four 4-hour exposures were 77 (6), 71 (8), 58 (4), and 21 (<2) ppm. Mortality was observed in the 71 (40%) and 77 (70%) ppm groups. All deaths occurred on the day of exposure. Clinical signs were observed on the day of exposure for all groups except the 21 ppm group and included hypoactivity, ataxia, prostration, and signs of respiratory irritation. Hypoactivity during exposure was the only clinical sign seen in rats in the 58 ppm group. Animals were observed for the 14-day post-exposure period, and had no clinical signs of toxicity. No macroscopic lesions were observed in the remaining rats that died or in the rats killed at the end of the 2-week recovery period.
Reference:	American Cyanamid Company (1988). Bushy Run Research Center Report # 51-611 (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003; also cited in TSCA fiche OTS0516617-1).
Reliability:	Klimisch code: 1a. This study was conducted under OECD guidelines.

Type:	**Inhalation LC_{50}**
Species/Strain:	Male and female rats/Sprague-Dawley
Exposure Time:	1 hour
Value:	92 ppm (confidence limits, 87-97 ppm)
Method:	OECD Guideline 403 "Acute Inhalation Toxicity" Each group, containing 5 male and 5 female rats, was exposed once for 1 hour to vapor dynamically generated from 2-amino-2,3-dimethylbutanenitrile. The chamber atmosphere was monitored for 2-amino-2,3-dimethylbutanenitrile and hydrogen cyanide.
GLP:	Yes
Test Substance:	2-Amino-2,3-dimethylbutanenitrile, 96% in toluene
Results:	The mean concentrations of 2-amino-2,3-dimethylbutanenitrile and (HCN) for the three 1-hour exposures were 109 (12), 75 (4), and 63 (3) ppm. Mortality was observed in the 109 ppm group (9/10 rats died). All deaths occurred on the day of exposure. Clinical signs were observed on the day of exposure for all groups except the

	63 ppm group and included hypoactivity, ataxia, prostration, and signs of respiratory irritation. Animals were observed for the 14-day post-exposure period and had no clinical signs of toxicity. Body weight gains were observed for all survivors on days 7 and 14. No macroscopic lesions were observed in the remaining rats that died or in the rats killed at the end of the 2-week period.
Reference:	American Cyanamid Company (1988). Bushy Run Research Center Report # 51-611 (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003; also cited in TSCA fiche OTS0516617-1).
Reliability:	Klimisch code: 1a. This study conducted under OECD guidelines.

Additional References for Acute Inhalation Toxicity: None Found.

Type:	**Dermal LD_{50}**
Species/Strain:	Male rabbits/New Zealand White
Exposure Time:	24 hours
Value:	23 mg/kg bw (confidence interval, 16-32 mg/kg)
Method:	Rabbits were individually quarantined 3 days prior to the test. Animals were fed *ad libitum* during quarantine and the study. On the day prior to test, the animals were shaved. Neat test substance was applied at doses of 12.5, 25, 50, 100, and 200 mg/kg to the shaved skin of 5 groups of 5 male albino rabbits, then covered with an occlusive wrap for 24 hours. The test site was wiped clean after a 24-hour exposure period. Animals were observed for physical condition and mortality on the day of test material application and twice daily for 14 days. Gross autopsy was not performed.
GLP:	No
Test Substance:	2-Amino-2,3-dimethylbutanenitrile, purity >95%
Results:	All deaths occurred within 24 hours of dose application. All of the animals in the 200, 100, and 50 mg/kg dose groups died. Three of 5 rabbits in the 25 mg/kg dose group died. Signs of toxicity observed in all animals at all dose levels included ataxia and prostration.
Reference:	American Cyanamid Company (1983). Acute Dermal Toxicity of CL 94, 194 (March 4) (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for

2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).

American Cyanamid Company (1988). TSCA Fiche OTS0516617.

Reliability: Klimisch code: 2e. This study was not conducted under GLP or OECD guidelines, but generally meets scientific standards, is well documented, and is accepted for assessment.

Additional References for Acute Dermal Toxicity:

Data from this additional source supports the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

American Cyanamid Company (1984). Toxicity Report A84-3 (cited in TSCA Fiche OTS0540156).

Type: **Dermal Irritation**

Species/Strain: Rats/Charles River CD (Sprague-Dawley derived)

Method: A 28-day repeated dermal neurotoxicity study was conducted to assess the potential of the test substance to cause systemic toxicity and adverse effects on the nervous system. The test substance was administered dermally to rats (5/sex/group) at concentrations of 0, 3, 10, and 30 mg/kg (0, 3.578, 11.932, and 35.775 µL/kg) for 6 hours/day, 5 days/week for 4 weeks. The test substance was applied by gentle inunction over the clipped area of unabraded skin. Dosages were adjusted at 3-day intervals to accommodate body weight changes. The treated area was covered with an impervious patch. After 6 hours, the patch was removed and the treated area thoroughly cleansed.

For additional details regarding methods for the subchronic study, refer to Section 5.1.2.

GLP: Yes

Test Substance: 2-Amino-2,3-dimethylbutanenitrile, purity 94.2%

Results: All rats survived the experimental period. Skin irritation, consisting of mild erythema, eschar formation, dry and/or flaky skin, and small sores were observed at the application site of rats in the 10 and 30 mg/kg dose groups. No significant irritation was seen in the rats in the 3 mg/kg dose group.

	For additional details regarding subchronic results of this study, refer to Section 5.1.2.
Reference:	American Cyanamid Company (1984). AC 94,149: A 28-Day Dermal Rat Neurotoxicity Study (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).
Reliability:	Klimisch code: 1b. This study was not conducted under OECD guidelines, but was conducted under GLP.

Additional References for Dermal Irritation: None Found.

Type:	**Dermal Sensitization:** No Data.

Type:	**Eye Irritation**
Species/Strain:	Rabbits/Strain not reported
Method:	The test substance (89 mg) was instilled into the eyes of rabbits. No additional details were reported.
GLP:	Unknown
Test Substance:	2-Amino-2-methylbutanenitrile, purity >95%
Results:	Instillation of 89 mg of the test substance into the eyes of rabbits resulted in the death of 5 of 6 rabbits tested. No additional data was reported.
Reference:	American Cyanamid Company (1988). TSCA Fiche OTS0516617.
Reliability:	Not assignable because insufficient study information was available.

Additional References for Eye Irritation: None Found.

5.2 Repeated Dose Toxicity

Type:	**28-Day Dermal**
Species/Strain:	Rats/Charles River CD (Sprague-Dawley derived)
Sex/Number:	Male and female/5 per sex per group
Exposure Period:	28 days
Frequency of Treatment:	6 hours/day, 5 days/week
Exposure Levels:	0, 3, 10, 30 mg/kg
Method:	A 28-day repeated dermal neurotoxicity study was conducted to assess the potential of the test substance to cause systemic toxicity and adverse effects on the nervous system. The test substance was administered dermally to

rats (5/sex/group) at concentrations of 0, 3, 10, and 30 mg/kg (0, 3.578, 11.932, and 35.775 µL/kg) for 6 hours/day, 5 days/week for 4 weeks. The test substance was applied by gentle inunction over the clipped area of unabraded skin. Dosages were adjusted at 3-day intervals to accommodate body weight changes. The treated area was covered with an impervious patch. After 6 hours, the patch was removed and the treated area thoroughly cleansed. Detailed observations, body weights, and food consumption values were recorded at 3-day intervals.

Animals were perfused with 10% buffered neutral formalin solution prior to necropsy. The weights of the liver, kidney, heart, thyroid glands, brain, and gonads were recorded.

GLP: Yes

Test Substance: 2-Amino-2,3-dimethylbutanenitrile, purity 94.2%

Results: All rats survived the experimental period. There were no overt signs of toxicity observed at any treatment level; body weight gain, diet consumption, hematology, and clinical chemistry values were comparable across all groups.

A statistically significant increase in absolute thyroid weights was observed in male rats at all treatment levels. Thyroid weights for females were somewhat increased, though not significantly. Relative thyroid weights were also somewhat increased at all levels in both sexes with a significant increase in males at the 3 mg/kg level. Subsequent histopathology failed to find any pathologic change that would account for this finding. No other significant organ weight changes were observed at any treatment level. No test article-related gross or microscopic lesions were observed in the tissue samples from the adrenal gland, bone marrow, brain, eye and optic nerve, heart, liver, kidneys, lung, ovary, skeletal muscle, sciatic nerve, skin, spinal cord, testes, thyroid glands, and uterus. There were no overt signs of neurotoxicity at any treatment level. Skin irritation, consisting of mild erythema, eschar formation, dry and/or flaky skin, and small sores were observed at the application site of rats in the 10 and 30 mg/kg dose groups. No significant irritation was seen in the rats in the 3 mg/kg dose group.

The authors of this study, therefore, concluded that the NOEL is 3 mg/kg. As the intent of the repeated exposure dermal study is to assess systemic toxicity following dermal application of the test material, and as no evidence of

	systemic toxicity was observed at the high dose, one could conclude that 30 mg/kg did not produce systemic toxicity or neurotoxicity and should be considered a NOEL.
Reference:	American Cyanamid Company (1984). AC 94,149: A 28-Day Dermal Rat Neurotoxicity Study (cited in Cytec Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).
Reliability:	Klimisch code: 1b. This study was not conducted under OECD guidelines, but was conducted under GLP.

Additional References for Repeated Dose Toxicity: None Found.

5.3 Developmental Toxicity: No Data.

5.4 Reproductive Toxicity: No Data.

5.5 Genetic Toxicity

Type:	***In vitro* Bacterial Reverse Mutation Assay**
Tester Strain:	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537
Exogenous Metabolic Activation:	With and without Aroclor induced rat liver S-9 (50 µl/plate S-9 preparation)
Exposure Concentrations:	0.1, 1, 10, 100 µg/plate (0.1 µL test substance/plate)
Method:	EPA OPPTS 870.5265
	The maximum concentration tested in the Ames *Salmonella* Plate assay with and without metabolic activation (S-9) using bacterial strains TA98, TA100, TA1535, and TA1537 was 5000 µg/plate. The positive controls were 2-aminoanthracene (2-AA), N-methyl-N-nitro-N-nitrosoguanidine (MNNG), 9-aminoacridine (9-AA), and 2-nitrofluorene (2-NF). The negative (solvent) control was ethanol.
GLP:	No
Test Substance:	2-Amino-2,3-dimethylbutanenitrile, purity not reported
Results:	Negative
Remarks:	The test substance was cytotoxic at 1000 and 5000 µg/plate. No evidence of base-pair substitution or frame-shift mutation was observed.
Reference:	American Cyanamid (1983). Ames Bacterial/Microsome Mutagenicity tests of CL 94,149 (March 4) (cited in Cytec

Industries, Inc. (2001). High Production Volume (HPV) Challenge Program Data Summary and Test Plan for 2-Amino-2,3-dimethylbutanenitrile (July), http://www.epa.gov/chemrtk/viewsrch.htm, accessed November 11, 2003).

Reliability: Klimisch code: 2e. This study was not conducted under GLP or OECD guidelines, but generally meets scientific standards, is well documented, and is accepted for assessment.

Additional Reference for *In vitro* Bacterial Reverse Mutation Assay:

Data from this additional source supports the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

American Cyanamid Company (1988). TSCA Fiche OTS0516617.

Type: ***In vitro* Clastogenicity Studies:** No Data.

Type: ***In vivo* Genetic Toxicity:** No Data.