

Provisional Peer-Reviewed Toxicity Values for

3-Amino-4-chlorobenzotrifluoride
(CASRN 121-50-6)

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COMMONLY USED ABBREVIATIONS

BMC	benchmark concentration
BMD	benchmark dose
BMCL	benchmark concentration lower bound 95% confidence interval
BMDL	benchmark dose lower bound 95% confidence interval
HEC	human equivalent concentration
HED	human equivalent dose
IUR	inhalation unit risk
LOAEL	lowest-observed-adverse-effect level
LOAEL _{ADJ}	LOAEL adjusted to continuous exposure duration
LOAEL _{HEC}	LOAEL adjusted for dosimetric differences across species to a human
NOAEL	no-observed-adverse-effect level
NOAEL _{ADJ}	NOAEL adjusted to continuous exposure duration
NOAEL _{HEC}	NOAEL adjusted for dosimetric differences across species to a human
NOEL	no-observed-effect level
OSF	oral slope factor
p-IUR	provisional inhalation unit risk
p-OSF	provisional oral slope factor
p-RfC	provisional reference concentration (inhalation)
p-RfD	provisional reference dose (oral)
POD	point of departure
RfC	reference concentration (inhalation)
RfD	reference dose (oral)
UF	uncertainty factor
UF _A	animal-to-human uncertainty factor
UF _C	composite uncertainty factor
UF _D	incomplete-to-complete database uncertainty factor
UF _H	interhuman uncertainty factor
UF _L	LOAEL-to-NOAEL uncertainty factor
UF _S	subchronic-to-chronic uncertainty factor
WOE	weight of evidence

PROVISIONAL PEER-REVIEWED TOXICITY VALUES FOR 3-AMINO-4-CHLOROBENZOTRIFLUORIDE (CASRN 121-50-6)

BACKGROUND

A Provisional Peer-Reviewed Toxicity Value (PPRTV) is defined as a toxicity value derived for use in the Superfund Program. PPRTVs are derived after a review of the relevant scientific literature using established Agency guidance on human health toxicity value derivations. All PPRTV assessments receive internal review by a standing panel of National Center for Environment Assessment (NCEA) scientists and an independent external peer review by three scientific experts.

The purpose of this document is to provide support for the hazard and dose-response assessment pertaining to chronic and subchronic exposures to substances of concern, to present the major conclusions reached in the hazard identification and derivation of the PPRTVs, and to characterize the overall confidence in these conclusions and toxicity values. It is not intended to be a comprehensive treatise on the chemical or toxicological nature of this substance.

The PPRTV review process provides needed toxicity values in a quick turnaround timeframe while maintaining scientific quality. PPRTV assessments are updated approximately on a 5-year cycle for new data or methodologies that might impact the toxicity values or characterization of potential for adverse human health effects and are revised as appropriate. It is important to utilize the PPRTV database (<http://hhpprtv.ornl.gov>) to obtain the current information available. When a final Integrated Risk Information System (IRIS) assessment is made publicly available on the Internet (www.epa.gov/iris), the respective PPRTVs are removed from the database.

DISCLAIMERS

The PPRTV document provides toxicity values and information about the adverse effects of the chemical and the evidence on which the value is based, including the strengths and limitations of the data. All users are advised to review the information provided in this document to ensure that the PPRTV used is appropriate for the types of exposures and circumstances at the site in question and the risk management decision that would be supported by the risk assessment.

Other U.S. Environmental Protection Agency (EPA) programs or external parties who may choose to use PPRTVs are advised that Superfund resources will not generally be used to respond to challenges, if any, of PPRTVs used in a context outside of the Superfund program.

QUESTIONS REGARDING PPRTVS

Questions regarding the contents and appropriate use of this PPRTV assessment should be directed to the EPA Office of Research and Development's National Center for Environmental Assessment, Superfund Health Risk Technical Support Center (513-569-7300).

INTRODUCTION

3-Amino-4-chlorobenzotrifluoride [synonyms: 2-chloro-5-trifluoromethylaniline; 2-chloro-5-trifluoromethyl-phenylamine; 2-chloro-5-(trifluoromethyl)aniline; 2-chloro-5-(trifluoromethyl)phenylamine; benzenamine, 2-chloro-5-(trifluoromethyl)] CASRN 121-50-6 is a clear liquid, colorless to light yellow, with a penetrating odor, synthetically produced and used in the chemical industry. It is stable under normal temperatures and pressures. 3-Amino-4-chlorobenzotrifluoride presents a solubility of 11 g/L at 60°C in water and is soluble in most of organic solvents. The decomposition products of this chemical includes hydrogen chloride, nitrogen oxides, carbon monoxide, carbon dioxide, and hydrogen fluoride gas (Merck KGaA, 2010; ChemExper, 2011). The molecular formula for 3-amino-4-chlorobenzotrifluoride is $C_7H_5ClF_3N$ (see Figure 1 for the structure). A table of chemico-physical properties is provided below (see Table 1).

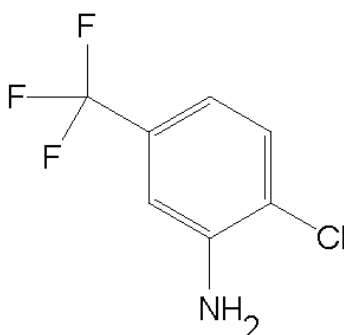


Figure 1. 3-Amino-4-chlorobenzotrifluoride Structure

Table 1. Physicochemical Properties (3-Amino-4-chlorobenzotrifluoride CASRN 121-50-6)^a	
Property (unit)	Value
Boiling point (°C)	82–83 (9 mmHg)
Melting point (°C)	10
Density (g/cm ³)	1.428 @ 20°C
Vapor pressure (mbar)	0.15
pH (unitless)	-
Solubility in water (g/L at 60°C)	11
Molecular weight (g/mol)	195.57

^aSources: Merck KGaA (2010), ChemExper (2011)

No Reference Dose (RfD), Reference Concentration (RfC), or cancer assessment for 3-amino-4-chlorobenzotrifluoride is included in the IRIS database (U.S. EPA, 2010) or on the Drinking Water Standards and Health Advisories List (U.S. EPA, 2009). No RfD or RfC values are reported in the Health Effects Assessment Summary Tables (HEAST; US. EPA, 2003). The Chemical Assessments and Related Activities (CARA) list (U.S. EPA, 1994) does not include a Health and Environmental Effects Profile (HEEP) for 3-amino-4-chlorobenzotrifluoride (U.S. EPA, 1985). The toxicity of 3-amino-4-chlorobenzotrifluoride has not been reviewed by the Agency for Toxic Substances and Disease Registry (ATSDR, 2010) or the World Health Organization (WHO, 2010). The California Environmental Protection Agency (CalEPA, 2008, 2009) has not derived toxicity values for exposure to 3-amino-4-chlorobenzotrifluoride. The American Conference of Governmental Industrial Hygienists (ACGIH, 2010) has not derived threshold limit value (TLV), nor biological exposure index; National Institute of Occupational Safety and Health (NIOSH, 2010) has cited neither a recommended occupational limit (REL), and Occupational Safety and Health Administration (OSHA, 2006b) has not cited permissible exposure limit (PEL) for 3-amino-4-chlorobenzotrifluoride. However, OSHA (2006a) does cite a PEL 8-hour time-weighted average (TWA) of 2.5 mg/m³ (3 ppm) for fluorides (as F), which is similar to the OSHA PEL for HF (as F) of 2.5 mg/m³ (3 ppm). NIOSH (2010) reports presents a REL of 2.5 mg/m³ (3 ppm) for HF, and ACGIH (2008) presents a TLV-TWA of 2.5 mg/m³ for fluorides, as F and TLV-TWA of 0.5 ppm, a ceiling limit of 2 ppm (skin) for HF.

The HEAST (U.S. EPA, 2003) does not report any values based on the U.S. EPA (1986) cancer weight-of-evidence classification for 3-amino-4-chlorobenzotrifluoride. 3-Amino-4-chlorobenzotrifluoride has not been evaluated under the 2005 *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005). The International Agency for Research on Cancer (IARC, 2010) has not reviewed the carcinogenic potential of 3-amino-4-chlorobenzotrifluoride. 3-Amino-4-chlorobenzotrifluoride is not included in the 11th Report on Carcinogens (NTP, 2005). CalEPA (2008) has not prepared a quantitative estimate of carcinogenic potential for 3-amino-4-chlorobenzotrifluoride.

Literature searches were conducted on sources published from 1900 through May 2011 for studies relevant to the derivation of provisional toxicity values for 3-amino-4-chlorobenzotrifluoride, CAS No. 121-50-6. Searches were conducted using EPA's Health and Environmental Research Online (HERO) database of scientific literature. HERO searches the following databases: AGRICOLA; American Chemical Society; BioOne; Cochrane Library; DOE: Energy Information Administration, Information Bridge, and Energy Citations Database; EBSCO: Academic Search Complete; GeoRef Preview; GPO: Government Printing Office; Informaworld; IngentaConnect; J-STAGE: Japan Science & Technology; JSTOR: Mathematics & Statistics and Life Sciences; NSCEP/NEPIS (EPA publications available through the National Service Center for Environmental Publications [NSCEP] and National Environmental Publications Internet Site [NEPIS] database); PubMed: MEDLINE and CANCERLIT databases; SAGE; Science Direct; Scirus; Scitopia; SpringerLink; TOXNET (Toxicology Data Network): ANEUP, CCRIS, ChemIDplus, CIS, CRISP, DART, EMIC, EPIDEM, ETICBACK, FEDRIP, GENE-TOX, HAPAB, HEEP, HMT, HSDB, IRIS, ITER, LactMed, Multi-Database Search, NIOSH, NTIS, PESTAB, PPBIB, RISKLINE, TRI; and TSCATS; Virtual Health Library; Web of Science (searches Current Content database among others); World Health Organization; and

Worldwide Science. The following databases outside of HERO were searched for risk assessment values: ACGIH, ATSDR, CalEPA, EPA IRIS, EPA HEAST, EPA HEEP, EPA OW, EPA TSCATS/TSCATS2, NIOSH, NTP, OSHA, and RTECS.

REVIEW OF POTENTIALLY RELEVANT DATA (CANCER AND NONCANCER)

The literature search revealed no human or animal studies (i.e., acute-, short-term-, subchronic-, or chronic-duration) for 3-Amino-4chlorobenzotrifluoride.

Doull et al. (1962) reported results of preliminary toxicity studies of 1200 compounds that included 3-amino-4-benzotrifluoride. The toxicity studies were necessary to determine the amount of each compound the mice could receive before the chemical toxicity caused death. Small group of mice were injected intraperitoneally with increasing dosage levels of each compound, and the resulting mortality was recorded for one week. The approximate LD₅₀ (lethal dose, 50%; 7-day) for 3-amino-4-benzotrifluoride was 100 mg/kg. No additional information was reported.

The Merck Safety Data Sheet (Merck KGaA, 2010) reported an *n*-octanol/water partition coefficient log P_{ow} of 3.19 for 3-amino-4-chlorobenzotrifluoride, which indicate a remarkable bioaccumulation potential. Also reported is an LC₅₀ (lethal concentration, 50%) of 7 mg/L for zebra fish (*Danio rerio*) for an exposure time of 96 hours and an EC₅₀ (Half maximal effective concentration 50) of 62 mg/L for bacteria for an exposure time of 3 hours (Merck KGaA, 2010). Another study by Dacarro et al. (1986), examined the toxicity of eight compounds (e.g., derivatives of benzotrifluoride and intermediates in the production of several herbicides) by a test based on the inhibition of the cell multiplication of *pseudomonas putida* that included 3-amino-4-chlorobenzotrifluoride. Through a mathematical model analogous to that proposed by Weiball, an EC₅₀ of over 100 mg/L was estimated (Dacarro et al., 1986).

DERIVATION OF PROVISIONAL VALUES

Limitations in the available data preclude development of cancer and noncancer toxicity values for 3-amino-4-chlorobenzotrifluoride.

CANCER WEIGHT-OF-EVIDENCE (WOE) DESCRIPTOR

Limitations in the available data preclude development of a WOE descriptor.

MODE-OF-ACTION (MOA) DISCUSSION

Limitations in the available data preclude determination of a MOA discussion.

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