

Provisional Peer-Reviewed Toxicity Values for

Guanidine Nitrate (CASRN 506-93-4)

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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 no-observed-adverse-effect level
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 no-observed-effect level
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 GUANIDINE NITRATE (CASRN 506-93-4)

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

Guanidine nitrate (CAS No. 506-93-4) is a strong oxidizer and chemically unstable (see Figure 1). It is explosive from friction, heat, or shock; it can ignite organic materials on contact; and, if heated to decomposition, it can emit toxic fumes of nitric acid and nitrogen oxide. The physicochemical properties are shown in Table 1. The chemical is used in the manufacture of explosives, disinfectants and photographic materials, and it is used as a monopropellant for some model airplane engines. Other salts of guanidine have other properties and uses. Guanidine chloride is a drug used to treat some rare neurologic diseases and in the laboratory as a protein denaturant. It is known to have immunosuppressive effects at or near therapeutic doses. Guanidine carbonate has a variety of uses, and the close relative melamine has uses in plastics and cosmetics, but it has caused nephrologic conditions in pets when used as a nitrogen additive in pet foods. The pharmaceutical target for the chloride derivative is aldehyde dehydrogenase (DrugBank, 2005). Guanidine nitrate is used as a propellant by the U.S. Army, which lists the chemical as slightly toxic with a mouse LD₅₀ of approximately 1100 mg/kg (Brown et al., 1988). The ecotoxicology data from the same source shows an EC₅₀ of 70.2 mg/L in Daphnia Magna, with a LOEC of 4.2 mg/L and a NOEC of 2.9 mg/L. In the less-sensitive species, fathead minnows (*Pimephales promelas*), the LOEC was 424 mg/L and the NOEC was 181 mg/L. There is additional ecotoxicology data available at <http://ecb.jrc.ec.europa.eu/iuclid-datasheet/506934.pdf>. Rat LD₅₀ values are available at the same source, and are in the same range as the mouse. An acute inhalation toxicity in the rat is also given as >0.853 mg/L (>0.853 mg/m³). Dermal exposure of rabbits produced only minor dermal irritation at 2 g/kg. No repeated-dose toxicology studies were found.

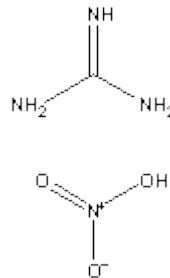


Figure 1. Guanidine Nitrate Structure

**Table 1. Physicochemical Properties Table
(Guanidine Nitrate CASRN 506-93-4)^a**

Property (unit)	Value
Boiling point (°C)	Decomposes
Melting point (°C)	213–215
Density (g/cm ³)	1.44
Vapor pressure (Pa at 25°C)	Not available
pH (unitless)	7
Solubility in water (g/100 mL at 20°C)	13
Relative vapor density (air = 1)	Not available
Molecular weight (g/mol)	122.08

^ahttp://www.chemicalbook.com/ProductChemicalPropertiesCB9150870_EN.htm

There could be some concern that the ingestion of quantities of guanidine nitrate could increase the nitrate load. Interested parties should consult the IRIS Nitrate document (available at www.EPA.GOV/IRIS) for additional information. No Reference Dose (RfD), Reference Concentration (RfC), or cancer assessment for guanidine nitrate 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; U.S. 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 guanidine nitrate (U.S. EPA, 1985). The toxicity of guanidine nitrate has not been reviewed by the Agency for Toxic Substances and Disease Registry (ATSDR, 2009) or the World Health Organization (WHO, 2010). The California Environmental Protection Agency (CalEPA, 2008, 2009) has not derived toxicity values for exposure to guanidine nitrate. No occupational exposure limits for guanidine nitrate have been derived by the National Institute of Occupational Safety and Health (NIOSH, 2005) or the Occupational Safety and Health Administration (OSHA, 2010). Mononitrate guanidine is included in the Hazardous Substances Data Bank as cited by the American Conference of Governmental Industrial Hygienists (ACGIH, 2010). This citation includes mention of human health effects (erythrocyte hemolysis in vitro, and respiratory and dermal toxicity in vivo), and nonhuman toxicity and ecotoxicity values, but it does not include human exposure limits.

The HEAST (U.S. EPA, 2003) does not report any values based on the EPA (1986) cancer weight-of-evidence (WOE) classification for guanidine nitrate. EPA has not reevaluated the chemical based upon the 2005 guidance (U.S. EPA, 2005). The International Agency for Research on Cancer (IARC, 2010) has not reviewed the carcinogenic potential of guanidine nitrate. Guanidine nitrate is not included in the *11th Report on Carcinogens* (NTP, 2005). CalEPA (2008) has also not prepared a quantitative estimate of carcinogenic potential for guanidine nitrate.

Literature searches were conducted on sources published from 1900 through May 2011, for studies relevant to the derivation of provisional toxicity values for guanidine nitrate (CAS No. 506-93-4). 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, HMTC, HSDB, IRIS, ITER, LactMed, Multi-Database Search, NIOSH, NTIS, PESTAB, PPBIB, RISKLINE, and TRI; 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 toxicity 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 repeated-dose human or animal studies (subchronic or chronic) for guanidine nitrate.

DERIVATION OF PROVISIONAL VALUES

Limitations in the available data preclude development of cancer and noncancer toxicity values.

DERIVATION OF SCREENING PROVISIONAL VALUES BASED ON A SURROGATE APPROACH

Several public databases (e.g., DSSTox, ChemIDplus) were screened for chemicals in support of a QSAR approach. There were no chemicals of >80% structural similarity. The standard procedure involves the identification of a surrogate chemical with sufficient structural similarity and sufficient in vivo outcome similarities on which to base an extrapolation. In this case, no significantly structurally similar compounds were identified, and no in vivo effects were available for comparison. Thus, a surrogate approach was not feasible.

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 an MOA discussion.

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