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Provisional Peer-Reviewed Toxicity Values for

2-Nitrodiphenylamine
(CASRN 119-75-5)

Superfund Health Risk Technical Support Center
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Questions regarding the contents of this document may be directed to the U.S. EPA Office of Research and Development's National Center for Environmental Assessment, Superfund Health Risk Technical Support Center (513-569-7300).

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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 2-NITRODIPEHNYLAMINE (CASRN 119-75-5)

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

2-Nitrodiphenylamine, CAS No. 119-75-5, is a solid, nitroaromatic compound used in the manufacture of fuel, propellants, and explosives (ATSDR, 1995). It is also used as a solvent dye. Although the human and animal health effects are unknown, 2-nitrodiphenylamine has been shown to enter the bloodstream via oral consumption of water or food. The distribution of 2-nitrodiphenylamine following inhalation or dermal exposure has not been examined. Figure 1 shows the chemical structure of 2-nitrodiphenylamine, and Table 1 presents the physicochemical properties of 2-nitrodiphenylamine.

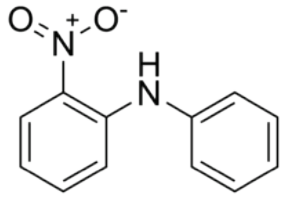

Figure 1. 2-Nitrodiphenylamine Structure (CASRN 119-75-5)

Table 1. Physicochemical Properties for **2-Nitrodiphenylamine** (CASRN 119-75-5)

Property (unit)	Value
Boiling point (ºC at 760 mmHg)	346[b]
Melting point (ºC)	75[a]
Density (g/cm^3)	1.36[b]
Vapor pressure (kPa at 20ºC)	Not available
pH (unitless)	5.0–7.0[c]
Solubility in water (mg/L at 25ºC)	27.7[d]
Relative vapor density (air = 1)	Not available
Molecular weight (g/mol)	214.223[a]
Flash point (°C)	Not available
Octanol/water partition coefficient (log K_{ow} unitless)	3.66[a]

[a]U.S. National Library of Medicine (2010); experimental data.
[b]ChemCAS (2010).
[c]Chemicalland21 (2010).
[d]U.S. National Library of Medicine (2010); estimated data.

No Reference Dose (RfD), Reference Concentration (RfC), or cancer assessment for 2-nitrodiphenylamine is included in the IRIS database (U.S. EPA, 2010a) 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, 2010b). The Chemical Assessments and Related Activities (CARA) list does not include a Health and Environmental Effects Profile (HEEP) for 2-nitrodiphenylamine (U.S. EPA, 1994). The toxicity of 2-nitrodiphenylamine 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 2-nitrodiphenylamine. No occupational exposure limits for 2-nitrodiphenylamine have been derived by the American Conference of Governmental Industrial Hygienists (ACGIH, 2010), the National Institute of Occupational Safety and Health (NIOSH, 2010), or the Occupational Safety and Health Administration (OSHA, 2010).

The HEAST (U.S. EPA, 2010b) does not report an EPA (1986) cancer weight-of-evidence (WOE) classification or an oral slope factor. The International Agency for Research on Cancer (IARC, 2010) has not reviewed the carcinogenic potential of 2-nitrodiphenylamine. 2-Nitrodiphenylamine is not included in the *11th Report on Carcinogens* (NTP, 2005). CalEPA (2008) has not prepared a quantitative estimate of carcinogenic potential for 2-nitrodiphenylamine.

Literature searches were conducted on sources published from 1900 through July 2011 for studies relevant to the derivation of provisional toxicity values for 2-nitrodiphenylamine, CAS No. 119-75-5. 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): ANEUPL, 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, 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, at any relevant exposure duration, available for hazard or dose-response assessment. However, the ATSDR published a Toxicological Profile for Otto Fuel II (ATSDR, 1995), of which 2-nitrodiphenylamine is a minor component. In this profile, limited information on the toxicity of 2-Nitrodiphenylamine alone was included. Following an acute oral exposure to 2-nitrodiphenylamine, a LD_{50} value of

6150 mg/kg was identified in rats (This information was obtained from a Material Safety Data Sheet on 2-nitrodiphenylamine [American Cyanamid, 1982], as cited in ATSDR, 1995). However, because the original acute study was unavailable for review, this value could not be verified by the ATSDR or the EPA. A U.S. Army review indicated that oral 2-nitrodiphenylamine exposure in rats at a dose of 3070 mg/kg resulted in an elevation of blood methemoglobin levels of 9.45% (U.S. Army, 1979; this information was obtained by the U.S. Army through personal communication with American Cyanamid). Because the actual study was unavailable for review, this information could not be verified by the ATSDR or the EPA. No other information pertaining to noncancer toxicity of 2-nitrodiphenylamine could be located.

DERIVATION OF PROVISIONAL VALUES

The lack of relevant data precludes development of both cancer and noncancer toxicity values.

CANCER WOE DESCRIPTOR

The lack of data precludes development of a WOE descriptor.

MODE-OF-ACTION DISCUSSION

The lack of data precludes development of a mode-of-action discussion.

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