

Provisional Peer Reviewed Toxicity Values for

2-Chloro-6-fluorophenol
(CASRN 2040-90-6)

Superfund Health Risk Technical Support Center
National Center for Environmental Assessment
Office of Research and Development
U.S. Environmental Protection Agency
Cincinnati, OH 45268

Acronyms and Abbreviations

bw	body weight
cc	cubic centimeters
CD	Caesarean Delivered
CERCLA	Comprehensive Environmental Response, Compensation and Liability Act of 1980
CNS	central nervous system
cu.m	cubic meter
DWEL	Drinking Water Equivalent Level
FEL	frank-effect level
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
g	grams
GI	gastrointestinal
HEC	human equivalent concentration
Hgb	hemoglobin
i.m.	intramuscular
i.p.	intraperitoneal
IRIS	Integrated Risk Information System
IUR	inhalation unit risk
i.v.	intravenous
kg	kilogram
L	liter
LEL	lowest-effect level
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
m	meter
MCL	maximum contaminant level
MCLG	maximum contaminant level goal
MF	modifying factor
mg	milligram
mg/kg	milligrams per kilogram
mg/L	milligrams per liter
MRL	minimal risk level
MTD	maximum tolerated dose
MTL	median threshold limit
NAAQS	National Ambient Air Quality Standards
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 inhalation reference concentration

p-RfD	provisional oral reference dose
PBPK	physiologically based pharmacokinetic
ppb	parts per billion
ppm	parts per million
PPRTV	Provisional Peer Reviewed Toxicity Value
RBC	red blood cell(s)
RCRA	Resource Conservation and Recovery Act
RDDR	Regional deposited dose ratio (for the indicated lung region)
REL	relative exposure level
RfC	inhalation reference concentration
RfD	oral reference dose
RGDR	Regional gas dose ratio (for the indicated lung region)
s.c.	subcutaneous
SCE	sister chromatid exchange
SDWA	Safe Drinking Water Act
sq.cm.	square centimeters
TSCA	Toxic Substances Control Act
UF	uncertainty factor
µg	microgram
µmol	micromoles
VOC	volatile organic compound

**PROVISIONAL PEER REVIEWED TOXICITY VALUES FOR
2-CHLORO-6-FLUOROPHENOL (CASRN 2040-90-6)**

Background

On December 5, 2003, the U.S. Environmental Protection Agency's (EPA's) Office of Superfund Remediation and Technology Innovation (OSRTI) revised its hierarchy of human health toxicity values for Superfund risk assessments, establishing the following three tiers as the new hierarchy:

1. EPA's Integrated Risk Information System (IRIS).
2. Provisional Peer-Reviewed Toxicity Values (PPRTV) used in EPA's Superfund Program.
3. Other (peer-reviewed) toxicity values, including:
 - ▶ Minimal Risk Levels produced by the Agency for Toxic Substances and Disease Registry (ATSDR),
 - ▶ California Environmental Protection Agency (CalEPA) values, and
 - ▶ EPA Health Effects Assessment Summary Table (HEAST) values.

A PPRTV is defined as a toxicity value derived for use in the Superfund Program when such a value is not available in EPA's Integrated Risk Information System (IRIS). PPRTVs are developed according to a Standard Operating Procedure (SOP) and are derived after a review of the relevant scientific literature using the same methods, sources of data, and Agency guidance for value derivation generally used by the EPA IRIS Program. All provisional toxicity values receive internal review by two EPA scientists and external peer review by three independently selected scientific experts. PPRTVs differ from IRIS values in that PPRTVs do not receive the multi-program consensus review provided for IRIS values. This is because IRIS values are generally intended to be used in all EPA programs, while PPRTVs are developed specifically for the Superfund Program.

Because science and available information evolve, PPRTVs are initially derived with a three-year life-cycle. However, EPA Regions or the EPA Headquarters Superfund Program sometimes request that a frequently used PPRTV be reassessed. Once an IRIS value for a specific chemical becomes available for Agency review, the analogous PPRTV for that same chemical is retired. It should also be noted that some PPRTV manuscripts conclude that a PPRTV cannot be derived based on inadequate data.

Disclaimers

Users of this document should first check to see if any IRIS values exist for the chemical of concern before proceeding to use a PPRTV. If no IRIS value is available, staff in the regional Superfund and RCRA program offices are advised to carefully review the information provided in this document to ensure that the PPRTVs used are appropriate for the types of exposures and circumstances at the Superfund site or RCRA facility in question. PPRTVs are periodically updated; therefore, users should ensure that the values contained in the PPRTV are current at the time of use.

It is important to remember that a provisional value alone tells very little about the adverse effects of a chemical or the quality of evidence on which the value is based. Therefore, users are strongly encouraged to read the entire PPRTV manuscript and understand the strengths and limitations of the derived provisional values. PPRTVs are developed by the EPA Office of Research and Development's National Center for Environmental Assessment, Superfund Health Risk Technical Support Center for OSRTI. Other EPA programs or external parties who may choose of their own initiative to use these PPRTVs are advised that Superfund resources will not generally be used to respond to challenges of PPRTVs used in a context outside of the Superfund Program.

Questions Regarding PPRTVs

Questions regarding the contents of the PPRTVs and their appropriate use (e.g., on chemicals not covered, or whether chemicals have pending IRIS toxicity values) may 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), or OSRTI.

INTRODUCTION

Verified toxicity values for 2-chloro-6-fluorophenol are unavailable on IRIS or HEAST (U.S. EPA, 2006, 1997). The chemical is not included in the Chemical Assessments and Related Activities (CARA) list (U.S. EPA, 1994, 1991). An ATSDR toxicological profile has not been produced for 2-chloro-6-fluorophenol (ATSDR, 2006a). Toxicity values for the chemical are not available from CalEPA (2006a, b). A health assessment for 2-chloro-6-fluorophenol is not available from the International Agency for Research on Cancer (IARC, 2006) or the World Health Organization (WHO, 2006). The chemical has not been assessed by the National Toxicology Program (NTP, 2006). Occupational guidelines and standards for 2-chloro-6-fluorophenol have not been established by the American Conference of Governmental Industrial Hygienists (ACGIH, 2005), the Occupational Safety and Health Administration (OSHA, 2006), or the National Institute for Occupational Safety and Health (NIOSH, 2006).

Research papers pertinent to the potential toxicological and carcinogenic effects of 2-chloro-6-fluorophenol were sought through computer searches of the CCRIS, GENETOX, HSDB, RTECS, and TSCATS databases (not date limited); DART/EPIC, MEDLINE,

TOXLINE, and TOXCENTER databases (1960's-May, 2006); and the Current Contents database (November, 2005-May, 2006).

REVIEW OF PERTINENT DATA

Human Studies

Available information regarding the toxicity of 2-chloro-6-fluorophenol in humans is limited to reports of sore throat, headache, eye irritation, nosebleeds, and skin rashes following exposure from an accidental atmospheric release of a mixture consisting mainly of 2-chloro-6-fluorophenol, toluene, and steam from a chemical facility near Holley, New York on January 5, 2002 (ATSDR, 2006b; NYSDOH, 2003; Juhl et al., 2003). The accident resulted in relocation of people from 15-20 homes in the area of greatest contamination. Follow-up consisted mainly of environmental and urine sampling. Environmental samplings were taken from air, soil, water, wipes from surfaces, vegetation, and miscellaneous household articles (ATSDR, 2006b; NYSDOH, 2003). Five rounds of urine sampling were performed, beginning on January 5, 2002 and ending in December, 2002 (ATSDR, 2006b). No reports of other human exposures to 2-chloro-6-fluorophenol were located. ATSDR (2006b) and NYSDOH (2003) noted the lack of information regarding the potential health effects of exposure to 2-chloro-6-fluorophenol and used available health effects data on chlorophenols to evaluate the potential health risks for exposure to 2-chloro-6-fluorophenol.

Animal Studies

No information was located regarding the health effects of exposure to 2-chloro-6-fluorophenol in animals.

FEASIBILITY OF DERIVING PROVISIONAL TOXICITY VALUES FOR 2-CHLORO-6-FLUOROPHENOL

Derivation of provisional toxicity values for 2-chloro-6-fluorophenol is precluded by the lack of quantitative human toxicity data, animal toxicity data, human or animal carcinogenicity data, and genotoxicity data for this chemical.

REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 2005. 2005 Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. ACGIH, Cincinnati, OH.

ATSDR (Agency for Toxic Substances and Disease Registry). 2006a. Searched June 19, 2006. <http://www.atsdr.cdc.gov/toxprofiles/>

ATSDR (Agency for Toxic Substances and Disease Registry). 2006b. Public Health Assessment. Diaz Chemical Corporation (A/K/A FMC C/O Diaz Chemical C/O FMC) Village of Holley, Orleans County, New York. Searched June 19, 2006.

http://www.atsdr.cdc.gov/hac/pha/diazchem/dcc_p1.html

CalEPA (California Environmental Protection Agency). 2006a. Chronic Reference Exposure Levels (RELs) and target organs. California Office of Environmental Health Hazard Assessment. Searched June 19, 2006.

<http://www.arb.ca.gov/toxics/healthval/chronic.pdf>

CalEPA (California Environmental Protection Agency). 2006b. Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. December 2, 2005. Searched June 19, 2006.

http://www.oehha.ca.gov/prop65/prop65_list/files/p65single120205.pdf

IARC (International Agency for Research on Cancer). 2006. Agents Reviewed by the IARC Monographs. Searched June 19, 2006.

<http://monographs.iarc.fr/ENG/Classification/Listagentscasnos.pdf>

Juhl, G.A., E.H. Kim and J.G. Benitez. 2003. A community exposure to 2-chloro-6-fluorophenol. Vet. Hum. Toxicol. 45:41-42.

NIOSH (National Institute for Occupational Safety and Health). 2006. Pocket Guide to Chemical Hazards. U.S. Department of Health and Human Services, Washington, DC. Searched June 19, 2006.

<http://www.cdc.gov/niosh/npg/npgsyn-c.html>

NTP (National Toxicology Program). 2006. Study Results and Research Projects. Searched June 19, 2006.

<http://ntp.niehs.nih.gov/index.cfm?objectid=720160DB-BDB7-CEBA-F7CC2DE0A230C920>

NYSDOH (New York State Department of Health). 2003. Public Health Assessment. Diaz Chemical Corporation January 5, 2002 Air Release. Available at:

<http://www.democratandchronicle.com/news/pdf/010403diaz.pdf>

OSHA (Occupational Safety and Health Administration). 2006. Table Z-1 Exposure Limits for Air Contaminants. Searched June 19, 2006.

http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=9992

U.S. EPA. 1991. Chemical Assessments and Related Activities (CARA). Office of Health and Environmental Assessment, Washington, DC. April.

U.S. EPA. 1994. Chemical Assessments and Related Activities (CARA). Office of Health and Environmental Assessment, Washington, DC. December.

U.S. EPA. 1997. Health Effects Assessment Summary Tables. FY-1997 Annual and FY-1997 Supplement. Office of Research and Development, Office of Emergency and Remedial Response, Washington, DC.

U.S. EPA. 2006. Integrated Risk Information System (IRIS). Online. Office of Research and Development, National Center for Environmental Assessment, Washington, DC.
<http://www.epa.gov/iris/>

WHO (World Health Organization). 2006. Alphabetical list of EHCs. Searched June 19, 2006.
http://www.who.int/ipcs/publications/ehc/ehc_alphabetical/en/index.html