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Provisional Peer Reviewed Toxicity Values for

Promethium
(CASRN 7440-12-2)

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 PROMETHIUM (CASRN 7440-12-2) AND PROMETHIUM SALTS

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 new information becomes available and scientific methods improve over time, PPRTVs are reviewed on a five-year basis and updated into the active database. 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

Promethium is the rarest of the rare earth elements that, as a class, also are referred to as lanthanides. In general, the lanthanides can be radioactive or stable. However, promethium probably does not occur in nature or in a stable form (Brzyska, 1996; Wells and Wells, 2001). Seventeen isotopes of promethium, with atomic masses from 134 to 155 were identified. Promethium-147, with a half-life of 2.6 years, generally was considered the most prevalent. Promethium-145 is the longest lived, with a half-life of 17.7 years (Lide, 2007). Primary decay products are neodymium (Nd) or samarium (Sm), depending on the isotope of promethium.

No toxicity or carcinogenicity assessments for promethium were available from IRIS (U.S. EPA, 2007), HEAST (U.S. EPA, 1997), CARA (U.S. EPA, 1991, 1994), or the Office of Water (U.S. EPA, 2006). Promethium had not been evaluated by ATSDR (2007) or IARC (2007), or tested or scheduled for testing by NTP (2007). A toxicological review of the lanthanides was identified, which derived toxicity values for several other lanthanides, but not for promethium or its compounds (TERA, 1999). No occupational exposure limits were recommended or promulgated for promethium by ACGIH (2007), NIOSH (2005), or OSHA (2007).

This document was based on information obtained through comprehensive searches of the following databases in June 1998 and 2007: TOXLINE (1965-2007), CANCERLINE (1970-2007), MEDLINE (1966-2007), GENETOX, DART, CCRIS, CHEMID, RTECS, EMIC,

ETICBACK, and TSCATS. Extensive tree-searching of acquired literature was performed to identify pertinent data from the older literature.

This document has passed the STSC quality review and peer review evaluation indicating that the quality is consistent with the SOPs and standards of the STSC and is suitable for use by registered users of the PPRTV system.

REVIEW OF PERTINENT LITERATURE

Human and Animal Studies

No data regarding the oral or inhalation toxicity of promethium were located in the available literature.

Human inhalation toxicity data on rare earth elements mainly consisted of case reports on workers exposed to multiple lanthanides (Kappenberger and Buhlmann, 1975; Husain et al., 1980; Sabbioni et al., 1982; Vocaturo et al., 1983; Colombo et al., 1983; Sulotto et al., 1986; Vogt et al., 1986; Waring and Watling, 1990; Deng et al., 1991). Animal inhalation toxicity data on rare earths mainly consisted of a few inhalation or intratracheal studies on some rare earth mixtures and some single compounds (Schepers, 1955a,b; Schepers et al., 1955; Ball and VanGelder, 1966; Abel and Talbot, 1967; Mogilevskaya and Raikhlin, 1967). However, because separation and purification procedures prior to the 1950s yielded impure lanthanides (Wells and Wells, 2001), we considered only those data generated since the newer purification methods were instituted.

The pulmonary toxicity of inhaled rare earth compounds, in general, have been the subject of debate, especially with regard to the relative contributions of radioactive contaminants versus stable elements in the development of progressive pulmonary interstitial fibrosis (Haley, 1991; Wells and Wells, 2001). In particular, although it was known that stable rare earth compounds could produce a static, foreign-body-type lesion consistent with benign pneumoconiosis, there was uncertainty whether they also could induce interstitial fibrosis that progressed after termination of exposure. A comprehensive assessment of the human and animal data by Haley (1991) concluded that the evidence suggested inhalation exposure to high concentrations of stable rare earths could produce lesions compatible with pneumoconiosis and progressive pulmonary fibrosis, and that the potential for inducing these lesions was related to chemical type, physiochemical form, dose, and duration of exposure. In a separate review, Hirano and Suzuki (1996) also concluded that chronic inhalation of lanthanide dusts probably caused pneumoconiosis in humans. However, no toxicity data specific to promethium were identified.

Other Relevant Data

The gastrointestinal absorption and distribution of promethium (^{147}Pm) was investigated in adult and neonatal (2-day-old) rats and neonatal (2-day-old) swine that were treated by gavage

and killed 1 week after treatment (Sullivan et al., 1984). Promethium was given as a single dose but the administered form, doses, and kind of solvent were not reported, although the pH of the solution was 2. Radioactivity was measured in the liver, kidney, and carcass of all animals; urine and lungs of adult and neonatal rats; and skin and GI tract of neonatal rats. Fecal levels of radioactivity were not determined. Total tissue retention after 7 days was 0.007, 5.4, and 3.4% of the administered dose in the adult rats, neonatal rats, and neonatal swine, respectively. Most of the dose retained by the neonatal rats was in the GI tract and skeleton (48.1% and 4.3% of administered dose, respectively). No toxicity endpoints were evaluated in this study. Hazards associated with ionizing radiation are not addressed here.

Carcinogenicity Data

No data regarding the carcinogenicity of promethium were located. Genotoxicity and other supportive data relating to the potential carcinogenicity of promethium were not located in the available literature. Hazards associated with ionizing radiation are not addressed here.

DERIVATION OF A PROVISIONAL SUBCHRONIC OR CHRONIC RfD FOR PROMETHIUM COMPOUNDS

Derivation of a p-RfD for promethium or its compounds was precluded by the lack of oral toxicity data.

DERIVATION OF A PROVISIONAL SUBCHRONIC OR CHRONIC RfC FOR PROMETHIUM COMPOUNDS

Derivation of a p-RfC for promethium or its compounds was precluded by the lack of inhalation toxicity data.

PROVISIONAL CARCINOGENICITY ASSESSMENT FOR PROMETHIUM COMPOUNDS

Weight-of-Evidence Descriptor

Available data on promethium or its compounds were insufficient for assessing possible carcinogenicity. In accordance with U.S. EPA (2005) guidelines for substances with inadequate human and animal data, promethium and its compounds were described as having "*inadequate information to assess carcinogenic potential*". Hazards associated with ionizing radiation are not addressed here.

Quantitative Estimates of Carcinogenic Risk

Derivation of an oral slope factor or inhalation unit risk for promethium or its compounds was precluded by the lack of data in humans and animals.

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