11-30-2001

Provisional Peer Reviewed Toxicity Values for

Chrysene

(CASRN 218-01-9)

Derivation of an Oral RfD

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 CHRYSENE (CASRN 218-01-9)
Derivation of an Oral RfD

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

An RfD for chrysene is not available on IRIS (U.S. EPA, 2001) nor in the HEAST (U.S. EPA, 1997). Chrysene is included on the Drinking Water Regulations and Health Advisory list as a B2 carcinogen; a noncancer health advisory is not available (U.S. EPA, 2000). The CARA database (U.S. EPA, 1991, 1994) lists a Health and Environmental Effects Profile (HEEP) (U.S. EPA, 1984), as well as a 1983 Reportable Quantity Document for Chrysene. The 1984 HEEP for Chrysene indicates that an Acceptable Daily Intake (ADI) was not estimated, due to the lack of chronic and subchronic data following exposure to chrysene by any route (U.S. EPA, 1984). The 1990 Drinking Water Criteria Document for PAH (U.S. EPA, 1990) did not contain information on the noncarcinogenic effects of chrysene. In 1995, ATSDR published a Toxicological Profile for PAHs in which only the carcinogenic effects of chrysene are discussed (ATSDR, 1995). NTP has not evaluated the noncarcinogenic toxicity of chrysene (NTP, 2001). ACGIH (2000) and WHO (1998) were searched for relevant information. Updated literature searches for oral noncancer data were conducted from 1989 to December 2000. The databases searched were:

TOXLINE, MEDLINE, CANCERLIT, CCRIS, TSCATS, HSDB, RTECS, GENETOX, DART/ETICBACK, and EMIC/EMICBACK.

REVIEW OF THE PERTINENT LITERATURE

Human Studies

Since the IRIS posting in 1990 (U.S. EPA, 2001), reviews by U.S. EPA (2000), ATSDR (1995), and WHO (1998) provided no data regarding the noncarcinogenic toxicity of chrysene in humans following oral exposure. The updated literature search identified no relevant studies regarding the noncarcinogenic toxicity of chrysene in humans following oral exposure.

Animal Studies

Since the IRIS posting in 1990 (U.S. EPA, 2001), reviews by U.S. EPA (2000), ATSDR (1995), and WHO (1998) provided no data regarding the noncarcinogenic toxicity of chrysene in animals following oral exposure. The updated literature search identified no relevant studies regarding the noncarcinogenic toxicity of chrysene in animals following oral exposure.

FEASIBILITY OF DERIVING A PROVISIONAL RfD FOR CHRYSENE

A provisional RfD for chrysene cannot be derived due to the lack of human data and animal data.

REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 2000. Documentation of Threshold Limit Values and Biological Exposure Indices, 6th ed. Cincinnati, OH. 1: 292-293.

ATSDR (Agency for Toxicological Substances Disease Registry). 1995. Toxicological Profile for PAH. U.S. Department of Health and Human Services, Public Health Service, Atlanta, GA.

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WHO (World Health Organization). 1998. Selected Non-Heterocyclic Polycyclic Aromatic Hydrocarbons. International Programme on Chemical Safety, Environmental Health Criteria Document No. 202.

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INTRODUCTION

A carcinogenicity assessment for chrysene is available on IRIS (U.S. EPA, 2001). This assessment, verified on 2/7/90, assigned chrysene to cancer weight-of-evidence group B2, probable human carcinogen, based on development of carcinomas and malignant lymphoma in mice after intraperitoneal injection, skin carcinomas in mice following dermal exposure, and chromosomal abnormalities in hamsters and mouse germ cells after gavage exposure. In support of these studies, positive responses in bacterial gene mutation assays and transformed mammalian cells exposed in culture have been observed with chrysene (U.S. EPA, 2001). Although there are no human data that specifically link exposure to chrysene with human cancers, chrysene is a component of PAH mixtures that have been associated with human cancer. These include coal tar, soots, coke oven emissions and cigarette smoke. Due to the lack of oral data, an oral slope factor was not derived (U.S. EPA, 2001). CRAVE Workgroup meeting notes provide no additional insight as to the potential for oral carcinogenicity of chrysene (U.S. EPA, 1990a, 1993a,b, 1994b). The HEAST (U.S. EPA, 1997) provides no other information. The B2

cancer weight-of-evidence classification is listed in the Drinking Water Standards and Health Advisories list without a health advisory quantification of cancer risk (U.S. EPA, 2000). The CARA list (U.S. EPA, 1991, 1994a) includes a Health and Environmental Effects Profile for Chrysene (U.S. EPA, 1984), as well as two reportable quantity documents for carcinogenic effects of chrysene (U.S. EPA, 1983, 1988). In the 1984 HEEP (U.S. EPA, 1984), the lack of available data regarding the carcinogenic effects of chrysene following oral exposure precluded derivation of a cancer quantitative estimate. The 1990 Drinking Water Criteria Document for PAH also considered the potential for carcinogenicity following exposure to chrysene; however, the oral route was not assessed (U.S. EPA, 1990b). An ATSDR Toxicological Profile for PAHs (ATSDR, 1995) did not include any information regarding carcinogenicity of chrysene following oral exposure. The International Agency for Research on Cancer (IARC, 1987, 2001) lists chrysene as a group 3 carcinogen, not classifiable as to its carcinogenicity to humans; only limited animal evidence exists. Neither WHO (1998) nor NTP (2001) provided any relevant information regarding the carcinogenic potential of chrysene by oral route. ACGIH (2000) lists chrysene as a confirmed animal carcinogen with unknown relevance to humans, but does not recommend a TLV specifically for chrysene. Updated literature searches for cancer data were conducted from 1989 to December 2000. The databases searched were: TOXLINE, MEDLINE, CANCERLIT, CCRIS, TSCATS, HSDB, RTECS, GENETOX, DART/ETICBACK, and EMIC/EMICBACK.

REVIEW OF THE PERTINENT LITERATURE

Human Studies

Since the IRIS posting in 1990 (U.S. EPA, 2001), reviews by U.S. EPA (1993a, 1993b, 1994b, 2000), ATSDR (1995), and WHO (1998) provided no data regarding the carcinogenicity of chrysene in humans following oral exposure. The updated literature search identified no relevant studies regarding the carcinogenicity of chrysene in humans following oral exposure.

Animal Studies

Since the IRIS posting in 1990 (U.S. EPA, 2001), reviews by U.S. EPA (1993a, 1993b, 1994b, 2000), ATSDR (1995), and WHO (1998) provided no data regarding the carcinogenicity of chrysene in animals following oral exposure. The updated literature search identified no relevant studies regarding the carcinogenicity of chrysene in animals following oral exposure.

Other Studies

The Drinking Water Criteria Document for Polycyclic Aromatic Hydrocarbons (U.S. EPA, 1990b) indicated that chrysene produced mutations in *Salmonella* and chromosomal aberrations and morphologic transformation in mammalian cells (U.S. EPA, 1990b). Updated literature searches revealed no new information regarding the genetic toxicity of chrysene.

FEASIBILITY OF DERIVING A PROVISIONAL ORAL SLOPE FACTOR FOR CHRYSENE

A provisional oral slope factor for chrysene cannot be derived because human and animal oral cancer data are lacking.

REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 2000. Documentation of Threshold Limit Values and Biological Exposure Indices.

ATSDR (Agency for Toxicological Substances Disease Registry). 1995. Toxicological Profile for PAH. U.S. Department of Health and Human Services, Public Health Service, Atlanta, GA.

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