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Provisional Peer-Reviewed Toxicity Values for

Tridymite
(CASRN 15468-32-3)

Superfund Health Risk Technical Support Center
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COMMONLY USED ABBREVIATIONS

BMC	benchmark concentration
BMCL	benchmark concentration lower bound 95% confidence interval
BMD	benchmark dose
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
POD	point of departure
p-OSF	provisional oral slope factor
p-RfC	provisional reference concentration (inhalation)
p-RfD	provisional reference dose (oral)
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 TRIDYMITE (CASRN 15468-32-3)

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

Tridymite, CASRN 15468-32-3, is a crystalline form of silica (SiO_2). Silica occurs as crystalline, amorphous, microcrystalline, and cryptocrystalline mineral forms that differ in terms of their structural and physicochemical properties (NIOSH, 1974; IARC, 1997); however, the most common forms of silica are cristobalite (CASRN 14464-46-1) and quartz (CASRN 14808-60-7). During industrial and naturally occurring processes, tridymite (usually in the form of quartz) is heated to create silica bricks or diatomaceous earth, respectively (NIOSH, 1974; IARC, 1997). Tridymite is also used in insulation, filtering media, and as a siliceous refractory material to line furnaces (NIOSH, 1974). Tridymite is naturally present in volcanic rocks and soils, which can result in exposure during mineral extraction (NIOSH, 1974; IARC, 1997). Table 1 summarizes the selected physicochemical properties for tridymite.

Table 1. Physicochemical Properties of Tridymite (CASRN 15468-32-3)[a]

Property (unit)	Value
Boiling point (ºF)	4046
Melting point (ºF)	3110
Density (g/cm^3)	2.66
Vapor pressure (mmHg at 25ºC)	0
Solubility in water (g/100 mL at 25ºC)	ND
Relative vapor density (air = 1)	ND
Molecular weight (g/mol)	60.1

[a]OSHA, 2011a.

ND = no data.

No reference dose (RfD), reference concentration (RfC), or cancer assessment for tridymite is included in the U.S. Environmental Protection Agency (U.S. EPA) Integrated Risk Information System (IRIS) (U.S. EPA, 2011a) or on the Drinking Water Standards and Health Advisories List (U.S. EPA, 2011b). 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 does not include a Health and Environmental Effects Profile (HEEP) for tridymite (U.S. EPA, 1994). The toxicity of tridymite has not been reviewed by the Agency for Toxic Substances and Disease Registry (ATSDR, 2012). The World Health Organization (WHO, 2000) published a Concise International Chemical Assessment Document (CICAD) on crystalline silica that considered quartz but did not consider experimental studies on the effects of tridymite. The California Environmental Protection Agency (CalEPA, 2008, 2012) set a chronic inhalation reference exposure limit (REL) of 3 $\mu g/m^3$ for respirable crystalline silica based on its effects on the respiratory system. However, CalEPA (2008, 2012) did not specify the forms of crystalline silica that are regulated or provide any CASRNs. The National Institute

for Occupational Safety and Health (NIOSH, 2010) set a time-weighted average (TWA) REL of 0.05 mg/m^3 for crystalline silica in the form of respirable dust, which it considers a potential carcinogen. For this REL, NIOSH (2010) listed cristobalite, quartz, and tridymite as synonyms and trade names and provided the general CASRN for silicon dioxide (CASRN 14808-60-7). NIOSH (2010) also set levels considered to be immediately dangerous to life or health (IDLH) as 25 mg/m^3 for tridymite. These limits were based upon effects to the eyes and respiratory system, including eye irritation, cough, dyspnea (difficulty breathing), wheezing, decreased pulmonary function, progressive respiratory symptoms (silicosis), and lung cancer (NIOSH, 2010). Based on the results of epidemiological and animal studies, NIOSH (1974) recommended setting exposure level standards for tridymite and cristobalite at one-half of those recommended for quartz. The Occupational Safety and Health Administration (OSHA, 2006) derived two equations for the calculation of two 8-hour TWA permissible exposure limits (PELs) for crystalline silica in the form of respirable quartz (10 $mg/m^3 \div [\% SiO_2 + 2]$) and quartz in the form of dust (30 $mg/m^3 \div [\% SiO_2 + 2]$). The 8-hour TWA PEL for tridymite was defined as one-half of the value calculated for quartz using the same equations (OSHA, 2006, 2011a). No occupational exposure limit for tridymite is current or recommended by the American Conference of Governmental Industrial Hygienists (ACGIH, 2011).

The HEAST (U.S. EPA, 2003) does not include a U.S. EPA (1986) cancer weight-of-evidence classification or an oral slope factor for tridymite. The International Agency for Research on Cancer (IARC, 1997) reviewed the carcinogenic potential of tridymite and determined that there is limited evidence from animal experiments to determine the carcinogenicity of tridymite. IARC (1997) evaluated all forms of silica for their carcinogenicities and found that there was sufficient evidence to determine the carcinogenicity of inhaled quartz or cristobalite that can occur due to exposure to occupational sources of silica. Likewise, in animals, only quartz and cristobalite have been found to have sufficient evidence of carcinogenicity (IARC, 1997). The *12th Report on Carcinogens* (NTP, 2011) classifies respirable-size crystalline silica as a known human carcinogen based on sufficient evidence of carcinogenicity in humans. No CASRNs were identified in this report, so it is unclear whether this determination is applicable to tridymite (NTP, 2011). Worker exposure to respirable crystalline silica is associated with elevated rates of lung cancer and silicosis (NTP, 2011). In rats, intratracheal instillation and inhalation exposure to respirable crystalline silica consistently causes lung cancer adenocarcinoma and squamous cell carcinoma, and single intrapleural or intraperitoneal injections of respirable crystalline silica cause lymphoma (NTP, 2011). CalEPA (2012) has not prepared a quantitative estimate of the carcinogenic potential of tridymite. In summary, while there are several toxicity values available for various forms of crystalline silica, toxicity values specific for tridymite are quite limited.

Literature searches were conducted on sources published from January 1, 1900 through February 12, 2012 for studies relevant to the derivation of provisional toxicity values for tridymite, CASRN 15468-32-3. Searches were conducted using U.S. 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 toxicity values: ACGIH, ATSDR, CalEPA, U.S. EPA IRIS, U.S. EPA HEAST, U.S. EPA HEEP, U.S. EPA OW, U.S. EPA TSCATS/TSCATS2, NIOSH, NTP, OSHA, and RTECS.

REVIEW OF POTENTIALLY RELEVANT DATA (CANCER AND NONCANCER)

Table 2 provides an overview of the relevant databases for information on tridymite and includes potentially relevant repeated short-term-, subchronic-, and chronic-duration studies. The literature search revealed no human or animal studies (i.e., acute-, short-term-, or chronic-duration) sufficient for development of toxicity values for tridymite. Table 3 provides a summary of available toxicity values for tridymite and other forms of crystalline silica. Table 4 provides a summary of other available studies on tridymite. None of the studies summarized herein provide information that is sufficient to derive provisional toxicity values for oral or inhalation exposure to tridymite.

Table 2. Summary of Potentially Relevant Data for Tridymite (CASRN 15468-32-3)

Category	Number of Male/Female, Strain, Species, Study Type, Study Duration	Dosimetry[a]	Critical Effects	NOAEL	BMDL/ BMCL	LOAEL	Reference	Comments
Human								
1. Oral								
Acute[b]	ND							
Short-term[c]	ND							
Long-term[d]	ND							
Chronic[e]	ND							
2. Inhalation								
Acute[b]	ND							
Short-term[c]	ND	ND	6 reported cases of silicosis	ND	NC	ND	Beskow, 1978	Workers exposed to kieselguhr (contains quartz, cristobalite, and tridymite); unknown exposure duration; information only available from the abstract.
Long-term[d]	ND	ND	Silicosis and dyspnea	ND	NC	ND	Hansen, 1983	Workers exposed to dust containing silicic acid in unacceptable concentrations that was mixed with quartz, cristobalite, and tridymite; information only available from the abstract.
Chronic[e]	ND	ND	Stomach and lung cancer	ND	NC	ND	Greenberg, 1986	Worker exposed to mixed dusts presumed to contain quartz, cristobalite, and tridymite; information only available from abstract.

Table 2. Summary of Potentially Relevant Data for Tridymite (CASRN 15468-32-3)

Category	Number of Male/Female, Strain, Species, Study Type, Study Duration	Dosimetry[a]	Critical Effects	NOAEL	BMDL/ BMCL	LOAEL	Reference	Comments
Animal								
			1. Oral					
Subchronic	ND							
Chronic	ND							
Developmental	ND							
Reproductive	ND							
Carcinogenic	ND							
			2. Inhalation					
Acute	30/0 Worcester white rat strain; single intrapulmonary injection; observation until natural death (up to 365 d)	200 mg/kg	High mortality (20/30) in first 120 d. Severe (Grade 5) lung fibrosis in the survivors.				King et al., 1953	Tridymite demonstrated greater mortality and fibrotic potency than other forms of silica.
	70 (sex not specified), Wistar, rat, intratracheal instillation of tridymite, observed 24 wk	50 mg	Cellular reaction to formation of argyrophil fibers.	ND	NC	ND	Kosztolányi et al., 1972	Raw data not provided; histological methods unclear; general poor reporting.

Table 2. Summary of Potentially Relevant Data for Tridymite (CASRN 15468-32-3)

Category	Number of Male/Female, Strain, Species, Study Type, Study Duration	Dosimetry[a]	Critical Effects	NOAEL	BMDL/ BMCL	LOAEL	Reference	Comments
	10-15/0, S-D, rat, intratracheal instillation of hydrofluoric acid-etched tridymite, observed 3, 6, and 12 mo	50 mg	3 mo: small interstitial macrophagic, nonconfluent granulomas; dust particles in alveoli 6 and 12 mo: increased volume of ganulomas; moderate central fibrosis; dust in alveolar spaces.	ND	NC	ND	Chiappino and Vig1iani, 1982	Animals kept in specific pathogen free conditions were compared with those exposed to bacteria. Bacterial exposure increased silicosis development.
Subchronic	ND							
Chronic	ND							
Developmental	ND							
Reproductive	ND							
Carcinogenic	16/16 WISTAR-derived rats Alderly Park strain; single intrapulmonary injection; observation until natural death	20 mg tridymite/rat; body weights not given	16 malignant lymphomas of the histiocytic type (MLHT) counted in 11 of 32 treated rats vs 0 tumors in 16/16 saline control rats. Distribution of tumors among males and females was not reported.				Wagner et al., 1980	Tridymite form of silica was more potent than other forms tested.
	20/20 AGUS AgB[1] rat strain; single intra injection; observation until natural death	20 mg tridymite/rat; body weights not given	2 MLHT/40 rats vs 0 MLHT in 8/4 saline controls.				Wagner et al., 1980	

Table 2. Summary of Potentially Relevant Data for Tridymite (CASRN 15468-32-3)

Category	Number of Male/Female, Strain, Species, Study Type, Study Duration	Dosimetry[a]	Critical Effects	NOAEL	BMDL/ BMCL	LOAEL	Reference	Comments
	12/12 PVG rat strain: single intrapulmonary injection; observation until natural death	20 mg tridymite/rat; body weights not given	2 MLHT/24 rats vs 0 MLHT in 8/4 saline controls.				Wagner et al., 1980	

[a]These values have not been converted to adjusted daily dose (ADD in mg/kg-d), human equivalent dose (HED in mg/kg-d), or human equivalent concentration (HEC in mg/m^3) units.
[b]Acute = exposure for ≤24 hr (U.S. EPA, 2002).
[c]Short-term = repeated exposure for >24 hr but ≤30 d (U.S. EPA, 2002).
[d]Long-term = repeated exposure for >30 d but ≤10% of the total lifespan (based on 70-yr typical lifespan) (U.S. EPA, 2002).
[e]Chronic = repeated exposure for >10% lifespan (U.S. EPA, 2002).

NC = not calculated; ND = no data; S-D = Sprague-Dawley.

Table 3. Available Toxicity Values for Tridymite (CASRN 15468-32-3) and Crystalline Silica (various CASRNs)

Site	RfV (date published)		Notes	Date Accessed
	Tridymite	Crystalline Silica, Various Forms		
ACGIH; 8-hr TWA, cancer classification	Withdrawn due to insufficient data (2008)	0.025 mg/m^3 (2008); suspected human carcinogen (2008)	Threshold limit values for α-quartz (14808-60-7, 1317-95-9) and cristobalite (14464-46-1).	9/22/11
ATSDR	NV	NV	None	9/22/11
CalEPA; chronic inhalation REL, Proposition 65	NV	3.0 µg/m^3 (2008); evidence of carcinogenicity (2012)	No CASRN provided; REL based on effects to the human respiratory system.	9/22/11
IARC	Limited evidence of toxicity in animals (1997)	Sufficient evidence of carcinogenicity in humans and animals (1997)	"Crystalline silica inhaled in the form of quartz or cristobalite from occupational sources is carcinogenic to humans."	9/22/11
NIOSH; 10-hr TWA, IDLH	NV; 25 mg/m^3 (2010)	0.05 mg/m^3 (2010); considered to be a potential occupational carcinogen (2010)	CASRN 14808-60-7 lists cristobalite, quartz, and tridymite as synonyms and trade names.	9/22/11
NTP	NV	Known to be a human carcinogen based on sufficient evidence of carcinogenicity in humans (2011)	No CASRN assigned.	9/22/11
OSHA; 8-hr TWA	Use half the value calculated from the formula for quartz (2006, 2011a)	Respirable quartz is either 250 mppcf divided by the value "%SiO_2 + 5" or 10 mg/m^3 divided by the value "%SiO_2 + 2"; total quartz is 30 mg/m^3 divided by the value "%SiO_2 + 2" (2011b)	None	9/22/11
U.S. EPA; HEEP	NV	Not available	None	9/22/11
U.S. EPA; CARA	NV	NV	None	9/22/11
U.S. EPA; HEAST	NV	NV	None	9/22/11
U.S. EPA; carcinogen	NV	NV	None	9/22/11
U.S. EPA; drinking water	NV	NV	None	9/22/11
U.S. EPA; IRIS	NV	NV	U.S. EPA conducted a noncancer health assessment of crystalline and amorphous silica (U.S. EPA, 1996).	9/22/11
WHO	NV	Concise International Chemical Assessment (CICAD) of crystalline silica and quartz (2000)	CICAD did not review studies on the other forms of silica.	9/22/11

NV = not available.

Table 4. Other Studies

Category	Number of Male/Female, Strain, Species, Study Type, Study Duration	Dosimetry	Effects	Comments	References
Sister Chromatid Exchange (SCE)	Human lymphocytes cultured in vitro with and without monocytes	0, 0.5, 5.0, 50 µg tridymite/cm^2 of culture dish	Slightly but statistically significantly elevated SCEs at 50 µg tridymite/cm^2 only in the presence of monocyte coculture	No effect of tridymite on pure lymphocyte cultures.	Pairon et al. (1990)
DNA strand breakage	In vitro incubation of tridymite and other forms of silica with λ *Hind*III digest DNA or PM2 supercoiled DNA	Silica samples standardized by surface area of particles at 0.03 m^2/mL	Human DNA strand breaks; Thymine glycol production; Hydroxyl radical generation	Most results were not quantified. Relative potency of tridymite is midrange for most endpoints compared with other forms of silica.	Daniel et al. (1995)

DERIVATION OF PROVISIONAL VALUES

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

CANCER WEIGHT-OF-EVIDENCE (WOE) DESCRIPTOR

Limitations in the available data preclude development of a WOE descriptor for tridymite.

MODE-OF-ACTION (MOA) DISCUSSION

Limitations in the available data preclude determination of a MOA discussion.

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