Global Risk Resources



ITER & RiskIE Databases

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Toxicology Excellence for Risk Assessment (TERA)

Who is TERA?

Toxicology Excellence for Risk Assessment (*TERA*) is a non-profit 501(c)(3) corporation organized for scientific and educational purposes.

TERA's mission is to protect public health by developing and communicating risk assessment information, sponsoring peer reviews and consultations, improving risk methods through research, and educating the public on risk assessment issues.

TERA was founded in 1995 by former U.S. Environmental Protection Agency (EPA) staff with collectively 45+ years experience working in risk assessment and EPA's IRIS.

TERA's Activities Include:

- Developing human health risk values and improving methods for risk assessment
- •Conducting expert peer consultation and peer review of risk values, methods and research
- ■Compiling and distributing peer reviewed risk values through the *ITER* database; providing a notification system for in progress work through the RiskIE database; and offering collaboration opportunities and support via the Alliance for Risk Assessment
- Educating diverse groups on risk assessment through training courses and scientific support
- ■Donating 5% of annual staff time to pro bono activities

ITER

International Toxicity Estimates for Risk

Database of chronic human health risk values and cancer classifications from organizations around the world for 650+ chemicals

- Risk value data in a side-by-side table format
- A synopsis that explains the underlying basis and rationale for each risk value and differences in risk values
- A link to each organization's website or source document
- A forum through which independent parties can share their peer reviewed risk values
- A resource to ensure that risk managers do not "miss" useful data

Why do we need ITER?

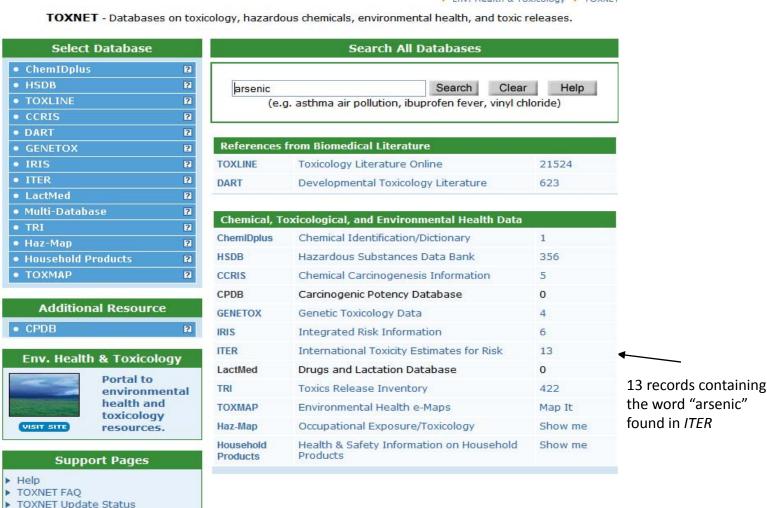
- Risk values are derived by a variety of organizations and may differ due to scientific judgments, methods, and/or availability of new data
- Organizations have different chemical priority lists and therefore, derive values for different chemicals
- Each agency publishes its work in printed documents and/or on its website; thus,
 risk assessors must search several websites, databases, and documents for data
- Non-governmental entities also derive values for chemicals, but do not typically have an avenue to make them publicly available
- TERA created ITER in 1996 to provide risk assessors and managers easy access to current international risk information from multiple organizations, to help its users understand differences in risk values derived by different organizations, and to provide a forum for independent parties to share their peer reviewed risk values

ITER Contains Data From:

- Agency for Toxic Substances & Disease Registry (ATSDR) Toxicological Profiles [http://www.atsdr.cdc.gov/toxpro2.html]
- Health Canada Priority Substances Assessment Reports [http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index_e.html]
- International Agency for Research on Cancer (IARC) Monographs [http://monographs.iarc.fr/] (in progress)
- NSF International Oral Risk Assessment Documents [http://www.nsf.org]
- National Institute of Public Health & the Environment (RIVM), The Netherlands – Maximum Permissible Risk Level Reports [http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf]
- U.S. Environmental Protection Agency (U.S. EPA) –IRIS [http://www.epa.gov/iris/index.html]
- Independent parties whose risk values have undergone independent peer review [http://www.tera.org/peer]

Arsenic Search in All TOXNET Databases





Fact Sheet

Database Description
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Save Checked Items

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TOXNET Home

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ITER S	earch Results Env. Health & Toxicology TOXNET
	Search Clear Limits
arsenic	
or chemi	icals, add synonyms and CAS numbers to search: Yes No
ems 1 thr	ough 13 of 13
	Names are sorted in <u>relevancy ranked</u> order.
Coloct	
Select Record	Substance Name
he follow	ing is the primary record for the chemical. All of the query terms were found.
1 🗆	ARSENIC, INORGANIC
• 🗀	Synonym: arsenic Primary record
	7440-38-2
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3 🗌	CACODYLIC ACID (DIMETHYLARSINIC ACID, DMA) 75-60-5
4 🗌	MONOMETHYLARSONIC ACID (MMA) 124-58-3
5 🗌	ROXARSONE 121-19-7
6 🗆	DICHLOROACETIC ACID 79-43-6
7 🗌	CADMIUM, INORGANIC 7440-43-9
8 🗌	NICKEL CHLORIDE 7718-54-9
9	BENZENE 71-43-2

ARSINE 7784-42-1





= Chemical evaluated and ITER data online.

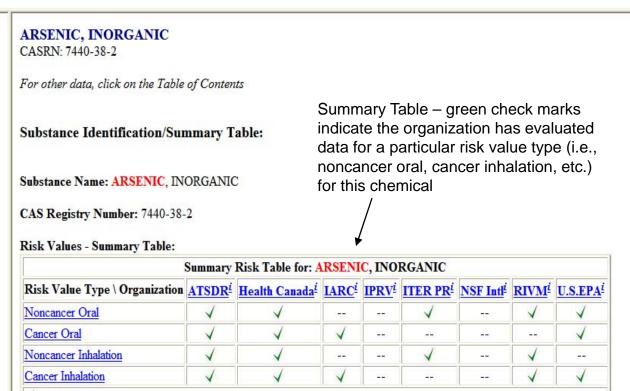




Table of Contents	Contract all categories Expand all categories Select Clear
☐ FULL RECORD	
BEST SECTIONS	
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Risk Values - Summary Table	•
Risk Data	
Risk Data - Noncancer Oral	
Risk Data - Cancer Oral	
Risk Data - Noncancer Inhalati	ion
Risk Data - Cancer Inhalation	
U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894,	
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Arsenic, Inorganic - Noncancer Oral Data

Risk Data - Noncancer	

ITER Noncancer Oral Risk Table for: ARSENIC, INORGANIC								
Risk Value Parameter\ Organization	<u>ATSDR</u> ⁱ	<u>Health</u> <u>Canadaⁱ</u>	<u>IARC</u> ^{<u>i</u>}	<u>IPRV</u> <u>i</u>	$\frac{\underline{\mathbf{ITER}}}{\underline{\mathbf{PR}}^{\underline{i}}}$	NSF Intl ^{<u>i</u>}	<u>RIVM</u> ^{<u>i</u>}	<u>U.S.EPA</u> ^{<u>i</u>}
Risk Value Name	chronic MRL	NA			NA		TDI	RfD
Risk Value*	3E-4	NA			see below		1E-3	3E-4
Year	2007	1992			1999		2000	1993
Basis (Experimental)*	NOAEL 0.0008	NA			NA		NOAEL 0.0021	NOAEL 0.0008
Basis (Adjusted)*	NA	NA			NA		NA	NA
Uncertainty Factor	3	NA			NA		2	3
Critical Organ or Effect	skin	NA			NA		skin	skin
Species	human	NA			NA		human	human
Study	Tseng et al., 1968; Tseng, 1977	NA			NA		Health Council of The Netherlands, 1993	Tseng, 1977; Tseng et al., 1968
View Specifics:	Click here	Click here			Click here		Click here	Click here
*In mg/kg body weight per day, unless otherwise specified.								

Synopsis:

ATSDR, Health Canada, RIVM, and U.S. EPA have evaluated the noncancer oral toxicity data for inorganic arsenic. Health Canada did not derive a risk estimate for noncancer toxicity since carcinogenicity is considered the critical endpoint. Both EPA and ATSDR risk values are based on the same study and use the same choice of critical effect, NOAEL and uncertainty factor.

RIVM derived a tolerable daily intake (TDI) of 0.001 mg/kg-day for critical effects on the skin in humans. This value is based on a NOAEL of 0.0021 mg/kg-day that was derived by Vermeire et al. (1991) from the World Health Organization provisional maximum tolerable weekly intake (PTWI) of organic arsenic of 15 mg/kg bw/week for adults of 70 kg of body weight. This PTWI was derived from a LOAEL of chronic intake of 100 ug arsenic/L in drinking water by humans, assuming a daily intake of drinking water of 1.5 L/day. RIVM used uncertainty factor of 2 to compensate for observation errors in an epidemiological study. Thus, the TDI is derived as follows: (100 ug arsenic/L x 1.5 L/day) / (70 kg) / (2) = 1 ug/kg-day (0.001 mg/kg-day).

Elf Atochem North America, Inc. (under the ITER PR column) has evaluated the potential developmental effects of inorganic arsenic. An expert panel concluded that at the experimental oral and inhalation doses tested, which generated frank maternal toxicity and lethality, no prenatal structural effects were induced in laboratory animals. By the oral route (gavage and diet), developmental toxicity (post-implantation loss and/or decreased fetal weight) was seen only occasionally and at the highest dose level, which also induced maternal toxicity. An independent peer review panel, through the TERA ITER Peer Review program, has reviewed and reached consensus on the Elf Atochem work, thereby qualifying it for inclusion in this database.

Arsenic, Inorganic - Noncancer Oral Data (Continued 1)

More Information : Level 3

Organization Name: ATSDR

Determination of Critical

See MRL Worksheet in Toxicological Profile, Appendix A, pp. A-5 through A-6. Available at "http://www.atsdr.cdc.gov/toxprofiles/tp2-a.pdf".

Quantitative Estimate:

See MRL Worksheet in Toxicological Profile, Appendix A, pp. A-5 through A-6. Available at "http://www.atsdr.cdc.gov/toxprofiles/tp2-a.pdf".

Peer Review:

Effect:

The ATSDR Toxicological Profile has undergone internal agency reviews and has been externally reviewed by a peer review panel.

Bibliography:

Tseng, W.P., H.M. Chu, S.W. How, J.M. Fong, C.S. Lin and S. Yeh. 1968. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. J. Natl. Cancer.

Inst. 40(3): 453-463.

Tseng, W.P. 1977. Effects and dose-response relationships of cancer and Blackfoot disease with arsenic. Environ. Health Perspect 19:109-119.

For Further Information: ATSDR (Agency for Toxic Substances and Disease Registry). 2007. Toxicological Profile for Arsenic. U.S. Department of Health and Human Services, Public Health Service.

August. Available at http://www.atsdr.cdc.gov/toxprofiles/tp2.html

For the list of ATSDR minimal risk levels (MRLs), see http://www.atsdr.cdc.gov/mrls/index.html

More Information: Level 3

Organization Name: Health Canada

Determination of Critical Effect:

Ouantitative Estimate:

Peer Review:

The Health Canada supporting documentation and assessment were approved by an interdirectorate committee of the Health Protection Branch of Health Canada and were externally reviewed by Drs. A. Li-Muller and R.R. Weiler of the Ontario Ministry of Environment and Energy, Drs. H.J. Gibb and C. Chen of the U.S. Environmental Protection Agency, Drs. P. Enterline and G. Marsh of the University of Pittsburgh and staff of the Information Department of BIBRA Toxicology International. The supporting documentation was externally reviewed by Dr. I. Harding-Barlow, Consultant. Dr. S. Bartlett of the Biostatistics and Computer Applications Division of the Environmental health Directorate, Health Canada assisted in the development of the quantitative estimates of carcinogenic potency. Background documentation for the assessment was prepared by BIBRA Toxicology International

Data identified prior to 1992 were considered for inclusion in the Health Canada assessment.

Bibliography:

For Further Information:

Hughes, K., M.E. Meek and R. Burnett. 1994. Inorganic Arsenic: Evaluation of Risks to Health from Environmental Exposure in Canada. In: Environmental Carcinogenesis and Ecotoxicology Reviews, Part C of Journal of Environmental Science and Health. C12(2): 145-159.

Environment Canada, Health Canada. 1993. Priority substances list assessment report: arsenic and its compounds. Ottawa. Ministry of Public Works and Government Services. Available at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/psl1-lsp1/index e.html or at the Inquiry Centre at 1-800-668-6767 (in Canada) or 819-997-2800 (outside Canada).

Arsenic, Inorganic – Noncancer Oral Data (Continued 2)

More Information: Level 3

Organization Name: ITER PR

Determination of NOTE: An assessment of the potential developmental effects of inorganic arsenic was developed by Elf Atochem North America, Inc. An independent peer review panel through TERA's Critical Effect: ITER Peer Review program has reviewed and reached consensus on the Elf Atochem work, thereby qualifying it for inclusion in this database.

An expert panel convened by TERA on June 14, 1999 reviewed a series of studies sponsored by Elf Atochem North America, Inc. on the potential developmental effects of inorganic arsenic. The studies included a literature review (DeSesso et al., 1998) and a series of peer-reviewed papers describing new experimental data (Nemec et al., 1998; Holson et al., in press a; Holson et al., in press b; Stump et al., in press). The panel reviewed these materials and addressed six questions. A brief discussion of the arsenic developmental data is found below, followed by the six questions and the panel's unanimous responses to these questions. Further details of the panel's discussions and conclusions can be found elsewhere on the TERA web site (http://www.tera.org/peer).

Members of the expert panel were Dr. Kenneth Bailey (U.S. EPA, retired), Dr. Donald Bjerke (Procter & Gamble), Dr. Michael Dourson (TERA), Mr. John Fawell (National Centre for Environmental Toxicology, U.K., written comments only), Dr. E. Sidney Hunter, III (U.S. EPA, Office of Research and Development), Mr. Thomas Long (ChemRisk), Dr. B.K. Nelson (NIOSH), Dr. Rebecca Parkin (George Washington University), Dr. Jennifer Seed (EPA Office of Prevention, Pesticides and Toxic Substances), and Dr. Calvin Willhite (California EPA).

Inorganic arsenic has been commonly considered to be a teratogenic agent -- in particular, an agent which causes neural tube defects. This notion is based on numerous studies of the same design performed in hamsters, mice, and rats, primarily using intravenous or intraperitoneal injections. The sponsor conducted an examination of this older literature base, and concluded that it was not appropriate for determining whether inorganic arsenic poses a risk of developmental effects in humans (DeSesso et al., 1998).

The older studies were not designed for use in risk assessment; rather, they were designed to study the formation of neural tube defects. To that end, single, high doses of an agent known to cause these defects were administered, typically by intravenous or intraperitoneal injection, at a critical period in neural tube development. Dose-response relationships were not determined, and only small numbers of animals were used. In addition, methods and results (including maternal effects) were not clearly or completely described. As pointed out by two of the early researchers in this area, "a common mistake is to assume that the classical teratogenesis experimental results are transportable into environmental risk assessment. The experiments are not designed for that purpose." Rather, "[o]nce an effect is revealed, then it is subject for further experiments designed to mimic actual environmental exposure conditions: portal of entry, dose, continuous exposure, etc." (Mottet and Ferm, 1983, p. 113).

To address the question of human risk, one looks first to epidemiology. While there are twelve studies that address arsenic reproductive or developmental effects in some fashion, all twelve studies were ecologic in design. They investigated smelter environs, industrial facilities, and community drinking water. Inorganic arsenic was not the focus of most studies, and in fact, no measurements of arsenic exposure were made during pregnancy. The studies poorly controlled, or did not control for, confounding variables, including maternal exposures to other agents, smoking, alcohol use, age, health, nutritional status, socioeconomic status, and prenatal care. Only a limited subset of these studies looked at any particular reproductive or developmental endpoint. Thus, the existing epidemiologic studies are inadequate for determining whether inorganic arsenic exposure causes or even is associated with structural malformations or other developmental effects in humans.

Because the existing laboratory animal and epidemiology literature were not adequate to answer the question posed, Elf Atochem North America, Inc. sponsored and reported a series of new experimental studies in rats, mice, and rabbits. All studies complied with U.S. regulatory guidelines and Good Laboratory Practices. The studies used a dose-response design, with a concurrent control group and three or four dose groups selected based on preliminary range-finding studies.

Where can I find ITER?

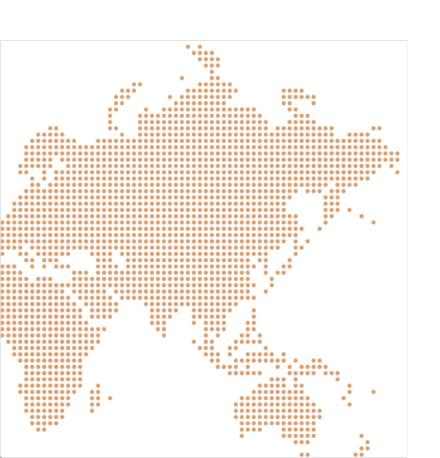
ITER is currently available in two locations:

- Original ITER http://www.tera.org/iter
- ITER on National Library of Medicine's TOXNET http://toxnet.nlm.nih.gov

The two locations contain the same information, however, the TOXNET display allows for additional search functions.

Edits to ITER are still made to the "Original ITER" location, which is uploaded to the TOXNET version of ITER on a weekly basis.

Risk Information Exchange



- A Database to Communicate In-Progress Risk & Toxicity Assessments
- Includes over 5100 projects being conducted by more than 25 organizations representing 13 countries
- Scheduled to join NLM's TOXNET in 2008

Why Do We Need RiskIE?

Chemical use and development has outpaced risk value development – RisklE ensures efficiency by helping:

- Identify opportunity for collaboration
- Eliminate duplication of effort

Risk assessment values vary across organizations – RisklE presents an opportunity for information exchange early in process

By providing a centralized source of project information, RiskIE aims to help bridge communication gaps among government, industry, academic, and environmental stakeholders of the risk assessment community

RiskIE helps organizations communicate!

RiskIE Contains Notifications From:

- Advisory Committee on Existing Chemicals (BUA)
- American Conference of Governmental and Industrial Hygienists
- American Industrial Hygiene Association
- Agency for Toxic Substances and Disease Registry
- California EPA's Office of Environmental Health Hazard Assessment (OEHHA)
- Department of the Environment (UK): Environmental Hazard Assessment
- Environment Canada
- European Chemicals Bureau
- Food Standards Agency (UK)
- Hawai'i Department of Health
- Health Canada
- International Agency for Research on Cancer
- Institution for Statutory Accident Insurance and Prevention in the Chemical Industry (BG Chemie)

... And From:

- International Programme for Chemical Safety
- Ministry of Health, Labour, and Welfare (Japan)
- National Academy of Sciences
- National Chemicals Inspectorate (Sweden)
- National Environmental Research Institute (Denmark)
- National Industrial Chemicals Notification and Assessment Scheme (Australia)
- National Resources Canada
- National Toxicology Program (NTP)
- Nordic Expert Group
- Organization for Economic Co-operation and Development (OECD)
- Occupational Safety and Health Administration (OSHA)
- Texas Commission on Environmental Quality (TCEQ)
- United States Environmental Protection Agency (USEPA)



RiskIE: Risk Information Exchange

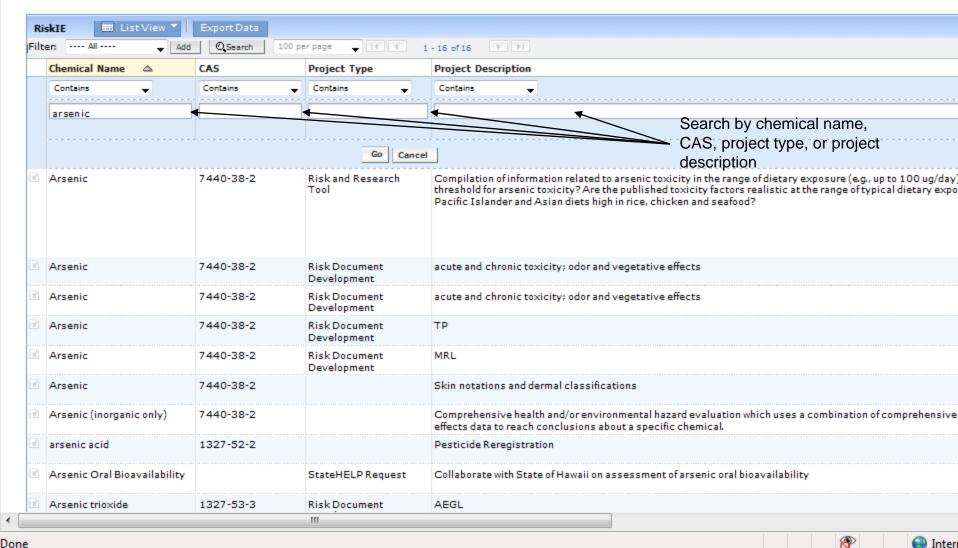
- · Organizations Included on RisklE
- Include your project on RisklE
- RisklE FAQ
- · Link to ITER

	er: All Add O Search 100 per p		1 - 100 of 5183		
	Chemical Name △	CAS	Project Type	Project Description	Status
eľ)	(2,4-Dichlorphenoxy) acetic acid	94-75-7	Risk Document Development	Proposition 65	In Progress
	(3-chloro-2-hydroxypropyl) trimethylammonium chloride	3327-22- 8	Risk Document Development	OEL	In Progress
ď	(3-Methylbutoxy)Acetic Acid, 2-Propenyl Ester	67634- 00-8	Risk Document Development	TAS	In Progress
	(Z)-octadec-9-enylamine	112-90-3	Risk Document Development	OEL	In Progress
m ²	1(3H)-Isobenzofuranone, 3,3-bis(4-hydroxyphenyl)-	77-09-8	Risk Document Development	Domestic Substance List: will then undergo a screening assessment for potential risks to human health or the environment.	In Progress
	1(3H)-Isobenzofuranone, 6-(dimethylamino)-3,3-bis [4-(dimethylamino)phenyl]-	1552-42- 7		Initial health and/or environmental hazard evaluation which uses a combination of data regarding toxic effects and limited exposure to reach an initial hazard assessment about a specific chemical.	In Progress
al'	1(3H)-Isobenzofuranone, 6-(dimethylamino)-3,3-bis [4-(dimethylamino)phenyl]-	1552-42- 7		Short-term testing for health effects	In Progress
	1,1'-(1,1-Dimethyl-3-methylene-1,3-propanediyl) bisbenzene	6362-80- 7	Risk Document Development	Short-term testing for health effects	In Progress
m ²	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl) bisbenzene	6362-80- 7	Risk Document Development	Initial health and/or environmental hazard evaluation which uses a combination of data regarding toxic effects and limited exposure to reach an initial hazard assessment about a specific chemical.	In Progress
al'	1,1'-Biphenyl	92-52-4		HPV Chemical Hazard Characterization	In Progress
="	1,1,1,2-Tetrachloro-2,2-difluoroethane	76-11-9	Risk Document Development	TLV	In Progress
	1,1,1-Trichloroethane	71-55-6		Toxicological Review	In Progress
al'	1,1,1-Trichloroethane	71-55-6		IRIS Toxicological Review	In Progress
	1,1,1-Trichloroethane	71-55-6	Risk Document Development	CNRV	Complet
ď	1,1,1-Trichloroethane	71-55-6	Risk Document Development	acute and chronic inhalation toxicity; odor and vegetative effects	In Progress

Arsenic Search in RiskIE

RiskIE: Risk Information Exchange

- Organizations Included on RisklE
- Include your project on RisklE
- RisklE FAQ
- Link to ITER



RiskIE - Arsenic, Individual Record View

Chemical Name:	Arsenic
CAS:	7440-38-2
Project Type:	Risk Document Development
Project Description:	acute and chronic inhalation toxicity; odor and vegetative effects
Status:	In Progress
Date of Completion:	
Organization:	Texas Commission on Environmental Quality
Contact:	rgrant@tceq.state.tx.us
Link:	http://www.tceq.state.tx.us/assets/public/implementation/tox/esl/consideration/2006.pdf
Last Verified:	10-Jun-2008 11:55:54

Where can I find RiskIE?

- RiskIE is currently available on the Alliance for Risk Assessment website at: <u>www.allianceforrisk.org/RiskIE.htm</u>
- RisklE is scheduled to join ITER on the National Library of Medicine's TOXNET database in 2008.

ITER and RiskIE Work Together

- ITER provides its users a "one stop shop" for viewing peer reviewed chronic human health risk values from around the world.
- RisklE provides an overview of the *in progress* risk values *and other* human health risk assessment work across the globe.
- As in progress risk values on RisklE are completed and peer reviewed, they graduate to *ITER*. Thus, if *ITER* does not include chronic risk values for a particular chemical, then search RisklE to find out what is underway.
- RiskIE also provides a big picture look at what projects are in the works in the overall field of human health risk assessment.

For More Information....

- About the ITER Database
 Contact Ms. Andrea Wullenweber at wullenweber@tera.org
 or (512) 863-5441
- About the RiskIE Database
 Contact Mr. Oliver Kroner at kroner@tera.org
 or (513)542-7475 ext. 19