Summary of Trichloroethylene (TCE) Inhalation Exposure Toxicity Values and Human Health Screening Levels

Inhalation Exposure Toxicity Values		
Source	**Non-Cancer**	**Cancer**
IRIS, USEPA updated 9/28/2011	RfC 2.0e-03 mg/m^3 Developmental, Immune Confidence High *The RfC was derived as the midpoint of two similar candidate RfCs—0.0019 mg/m3 for decreased thymus weight in mice (Keil et al., 2009) and 0.0021 mg/m3 for fetal heart malformations in rats (Johnson et al., 2003).*	IUR 4.1e-06 (µg/m^3)$^{-1}$ Mutagenic MOA, use ADAFs *- Extrapolation Method: Low-dose linear extrapolation from the point of departure (LEC01) with a factor of 4 applied to include non-Hodgkin's lymphoma (NHL) and liver cancer risks, combined risk* *- Tumor site(s): Hematologic, Hepatic, Urinary* *- Tumor type(s): Renal cell carcinoma, non-Hodgkin's lymphoma, and liver tumors (Charbotel et al. 2006 EPA, 2011 Raaschou-Nielsen et al., 2003)*
RSLs, USEPA May 2018 update	RfC 2.0e-03 mg/m^3 Source: IRIS	IUR 4.1e-06 (µg/m^3)$^{-1}$ Mutagen Source: IRIS
Inhalation Exposure Screening Levels		
Source	**Non-Cancer**	**Cancer**
RSLs, USEPA May 2018 update	Residential Exposure - 2.1 µg/m^3 Occupational Exposure – 8.8 µg/m^3	Residential Exposure - 0.48 µg/m^3 Occupational Exposure – 3.0 µg/m^3 - SLs utilize EPA default receptor exposure parameters
ATSDR MRLs June 2017 update	Chronic MRL 0.0004 ppm (= 2.1 µg/m^3) Intermediate MRL 0.0004 ppm (= 2.1 µg/m^3) - Endpoints (draft 10/14): developmental, UF 10 immunological, UF 100	[ATSDR does not calculate cancer slope factors]

Notes:
ADAF – USEPA Age-dependent Adjustment Factors applied to mutagenic carcinogens for age-specific cancer risk estimates
ATSDR – Agency for Toxic Substances and Disease Registry, U.S. DHHS
IRIS – USEPA Integrated Risk Information System
MRL – ATSDR Minimum Risk Levels
RSL - USEPA Regional Screening Levels, Superfund Program
SL – Screening Level

From: Adams, Glenn
To: Bateson, James
Cc: Koporec, Kevin; Frederick, Tim; Chan, Sydney
Subject: TCE
Date: Wednesday, November 9, 2016 7:13:51 PM

Jim,
Here is the information you requested about how we look at TCE in indoor air. I hope this is what you are looking for. Please let me know if you have any questions.
Glenn

Screening and Removal Management Levels for Volatile Organic Compounds

Contaminant	Residential RSL	Residential RML	Commercial RSL	Commercial RML
PCE	11 ug/m^3	126 ug/m^3	47 ug/m^3	540 ug/m^3
TCE	0.48 ug/m^3	6.3 ug/m^3	3 ug/m^3	26 ug/m^3
TCE (sensitive sub-population)[1]	0.48 ug/m^3	2.1 ug/m^3	3 ug/m^3	8.8 ug/m^3

The EPA has guidance and tables that present Regional Screening Levels (RSLs) and Removal Management Levels (RMLs) for contaminants at Superfund and RCRA sites. The links to these guidance documents and the tables are below. These documents discuss how, when, and where these values are appropriate to use.

Regional Screening Levels - RSLs are values used by the EPA to determine whether a chemical should be considered for further monitoring or investigation. They are conservative (protective) risk-based values calculated at a 10-6 risk level for carcinogens (1 excess cancer per 1,000,000 people) or a Hazard Quotient of 1 for non-carcinogens. Generally, if chemical concentrations are above an RSL, the EPA considers further investigation to determine the full nature and extent of any contamination.

RSLs website - http://www.epa.gov/risk/regional-screening-table

Removal Management Levels - RMLs are values used by the EPA to identify areas, contaminants, and conditions where an action may be necessary to protect human health and/or the environment. The RMLs are risk-based values calculated at a 10-4 risk level for carcinogens (1 excess cancer per 10,000 people) or a Hazard Quotient of 3 for non-carcinogens. These actions, determined on a site-specific basis, can vary depending on the contaminant and the concentration and could include such actions as interim measures to lessen exposure or active mitigation/treatment. Generally, if chemical concentrations are above an RML, the EPA considers appropriate exposure or treatment actions. Exceedance of an RML by itself does not imply that adverse health effects will occur.

RMLs website - http://www.epa.gov/risk/regional-removal-management-levels-chemicals-rmls

1- Region 4's Scientific Support Section (SSS) recommends a chemical specific RML for TCE in residential air of 2 ug/m3 (HQ of 1) and 8.8 ug/m3 (HQ of 1) for commercial/industrial air with sensitive populations (i.e., women of child bearing age) present. These concentrations are expected to be protective for potential non-cancer health effects, including developmental effects.

Glenn Adams, Chief
Scientific Support Section
EPA Region 4 Superfund Division
404-562-8771 (office)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 27 2014

OFFICE OF
SOLID WASTE AND
EMERGENCY RESPONSE

MEMORANDUM

SUBJECT: Compilation of Information Relating to Early/Interim Actions at Superfund Sites and the TCE IRIS Assessment

FROM: Robin H. Richardson, Acting Director
Office of Superfund Remediation and Technology Innovation (OSRTI)

TO: Superfund Division Directors, EPA Regions 1 - 10

Purpose

This compilation of information was prepared in response to requests from U.S. Environmental Protection Agency (EPA) Regional Offices. It provides information regarding existing EPA guidance on early or interim actions at Superfund sites. It also provides current information about the toxicity of trichloroethylene (TCE). The information referenced in this document may be used to support Superfund decision making at sites with actual or potential inhalation exposures to TCE.

Background

In September 2011, the U.S. Environmental Protection Agency (EPA) published a toxicological assessment for TCE[1]. Based upon a weight-of-evidence evaluation of the available information, including human epidemiologic studies, animal dosing studies, and experimental mechanistic studies, the assessment concluded that TCE poses a potential human health hazard for noncancer toxicity to the central nervous system, kidney, liver, immune system, male reproductive system, and the developing fetus, and is "carcinogenic to humans" by all routes of exposure. The assessment for IRIS derived a chronic inhalation reference concentration (RfC) for noncancer effects of TCE, which is two micrograms per cubic meter (2 $\mu g/m^3$). This RfC is based in part on the developmental toxicity endpoint of increased incidence of fetal cardiac malformations.

Early or Interim Action for TCE

In considering how the 2011 TCE IRIS assessment should be used in Superfund decision making, the existing Federal statutes and EPA guidance offer the following:

[1] U.S. EPA (2012). *Toxicological Review of Trichloroethylene in Support of the Integrated Risk Information System (IRIS).* Currently available online at: http://www.epa.gov/iris/toxreviews/0199tr/0199tr.pdf.

- *Early or interim actions:* EPA expects to take early actions at Superfund sites where appropriate to eliminate, reduce, or control the hazards posed by a site. In assessing such cases, EPA will act with a bias for initiating response actions to ensure protection of human health[2].
- *Considering noncancer health effects:* For purposes of the Superfund program and consistent with the National Oil and Hazardous Substances Pollution Contingency Plan (NCP), unacceptable risk occurs when exposures exceed concentrations to which the human population, including sensitive subgroups, may be exposed without adverse effect during a lifetime or part of a lifetime, as appropriate to address teratogenic and developmental effects[3].
- *Developmental toxic effects*: In most cases, it is assumed that a single exposure at any of several developmental stages may be sufficient to produce an adverse developmental effect,[4] but the RfC for a single exposure hasn't been determined yet by EPA.
- *IRIS Database*: IRIS normally represents the official Agency scientific position regarding the toxicity of the chemicals based on the data available at the time of the review and is the generally preferred source of human health toxicity values used to support Superfund response decisions[5]. For noncancer effects, a concentration of 2 $\mu g/m^3$ TCE in indoor air is expected to be a reasonable maximum exposure condition for a continuous chronic exposure to prevent risk of adverse health effects during a lifetime.
- *Risk Assessment Guidance for Superfund: Volume I Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment)* [6] addresses the use of inhalation toxicity values in Superfund risk assessments, including discussion of estimating exposures in microenvironments[7] by calculating time-weighted average exposures concentrations for each exposure period characterized by a specific activity pattern. It also recognizes that chemical-specific elements of metabolism and kinetics, reversibility of effects, and recovery time should be considered when defining the duration of a site-specific exposure scenario.
- *ARARS*: At sites contaminated with TCE addressed by CERCLA, additional (non-EPA) TCE concentration or toxicity values may exist that could represent applicable or relevant and appropriate requirements (ARARs), including more stringent state standards or policy.[8]

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[2] National Oil and Hazardous Substances National Contingency Program (NCP) ((see 40 CFR 300.415 (b)(1)-(3) and 300.430 (a)(1)(ii)(A)).

[3] U.S. EPA (1991). *Role of the Baseline Risk Assessment in Superfund Remedy Selection Decisions.* OSWER Directive 9355.0-30. Currently available on-line at: http://www.epa.gov/oswer/riskassessment/pdf/baseline.pdf

[4] U.S. EPA (1991). *Guidelines for Developmental Toxicity Risk Assessment* (EPA/600/FR-91/001) describes the procedures that EPA follows in evaluating potential developmental toxicity associated with human exposure to environmental agents. Currently available online at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=23162

[5] U.S. EPA (2003) *Human Health Toxicity Values in Superfund Risk Assessments* (OSWER Directive 9285.7-53). Currently available online at http://www.epa.gov/oswer/riskassessment/pdf/hhmemo.pdf

[6] U.S. EPA (2009). *Risk Assessment Guidance for Superfund: Volume I Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment.* This document is currently available on-line at: http://www.epa.gov/oswer/riskassessment/ragsf/pdf/partf_200901_final.pdf

[7] U.S. EPA (2004). *Air Quality Criteria for Particulate Matter: Volume II.* Microenvironments are defined as a space that can be treated as a well-characterized, relatively homogeneous location with respect to pollutant concentration for a specified time period (e.g., rooms in homes, restaurants, schools, offices, inside vehicles, or outdoors). Currently available online at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=95398

[8] For a description of ARARs, see, for example: http://www.epa.gov/superfund/policy/remedy/sfremedy/arars.htm

Summary

Existing guidance provides that responders should consider *early or interim* action(s) where appropriate to eliminate, reduce, or control the hazards posed by a site. In doing so, IRIS generally provides the best available toxicological information in support of *early or interim* action for buildings where investigations of indoor air contamination identify site-related concentrations of TCE.

Additional Information

Additional information related to vapor intrusion and existing OSWER guidance can be found at http://www.epa.gov/oswer/vaporintrusion/ and http://www.epa.gov/oswer/riskassessment/. Please contact Michael Scozzafava (Chief, Science Policy Branch) at (703) 603-8833 if you have questions or require further information.

cc: Mathy Stanislaus, OSWER/IO
Nitin Natarajan, OSWER/IO
Barry Breen, OSWER/IO
Reggie Cheatham, OSWER/OEM
David Lloyd, OSWER/OBLR
Charlotte Bertrand, OSWER/FFRRO
Carolyn Hoskinson, OSWER/OUST
Kent Benjamin, OSWER/IPCO
Barnes Johnson, OSWER/ORCR
Nigel Simon, OSWER/OPM
Cyndy Mackey, OECA/OSRE
John Michaud, OGC/SWERLO
Franklin Hill, OSWER/OSRTI
Dana Stalcup, OSWER/OSRTI
Michael Scozzafava, OSWER/OSRTI
Richard Kapuscinski, OSWER/OSRTI
Barbara Hostage, OSWER/PARMS
Stiven Foster, OSWER/PARMS

North Carolina Division of Waste Management
Supplemental Vapor Intrusion Guidance

Trichloroethylene (TCE) Indoor Air Inhalation Immediate Action Levels and Response

February 2, 2017

Introduction

In 2011, the U.S. Environmental Protection Agency's (USEPA) Integrated Risk Information System (IRIS) (http://www.epa.gov/iris) issued an update to the toxicological evaluation for trichloroethylene (also known as trichloroethene or "TCE"). In that update [TCE 2011], IRIS established revised toxicity values for oral and inhalation exposures to TCE. The current North Carolina Department of Environmental Quality (DEQ) Division of Waste Management (DWM) Preliminary Soil Remediation Goals (PSRG) and vapor intrusion screening levels reflect the revised IRIS values. In addition to the vapor intrusion screening levels, DWM has established additional indoor air inhalation exposure immediate action levels (Table 1) for TCE to protect sensitive populations (groups of people most likely to suffer adverse health effects) from short-term exposures that may result in long-term effects.

The TCE-sensitive population for short-term exposures is women of child-bearing age, defined as women of age 15–50 years, although site-specific consideration of the appropriate age range should be evaluated in concert with the exposed women and DWM. **When it is identified that TCE-sensitive populations may be exposed to concentrations greater than the DWM action levels found in Table 1, immediate steps are to be taken to eliminate the exposure or reduce the exposure concentration to less than the action level.**

Table 1. Division of Waste Management (DWM) Immediate Action Levels for Trichloroethylene (TCE) Inhalation Exposures

Exposure Scenario	TCE Action Level - Inhalation	Required Action by the State-Lead Contractor, Consultant or Remediation Party [1]
Residential	2.1 µg/m^3 (0.39 ppbv)	1. Notify DWM within 1 business day 2. Immediately provide fact sheets to potentially affected individuals and involve DWM 3. Initiate measures to reduce exposure below the action level immediately.
Non-residential	8.8 µg/m^3 (1.6 ppbv)	
TCE sensitive populations are defined as: Women of child-bearing age (15 to 50 years of age) [2]		

[1] The required action time frame begins when the remediating party, DWM State-Lead Program or Brownfields Program applicant's receives the validated laboratory data

[2] A site-specific evaluation of the appropriate age range for women of child-bearing age should be made in consultation with the exposed women and DWM

TCE = trichloroethylene (trichloroethene, CASN 79-01-6)

The USEPA IRIS toxicological review identifies as one of the non-cancer critical health effects for TCE as fetal cardiac malformations. Because cardiac development begins during the earliest stages of fetal development, at a time before a woman may realize she is pregnant, TCE exposure to women during their first trimester of pregnancy is of particular concern Permanent adverse effects to fetal cardiac development may occur as a result of short-term maternal exposures. The USEPA identifies that a single fetal exposure to a developmental toxicant may be sufficient to produce an adverse developmental effect (EPA 2014b). DWM's TCE short-term inhalation action levels are developed from the USEPA IRIS reference concentration (RfC) of 2.0 µg/m^3 [TCE 2011]. The DWM action levels found in Table 1 are equivalent to the USEPA TCE regional screening levels (RSLs) (https://www.epa.gov/risk/regional-screening-levels-rsls) for residential and "composite worker" (non-residential) exposure.

If TCE is a chemical currently in use in the building being investigated for vapor intrusion, the Occupational Safety and Health Administration (OSHA) standards govern the amount of chemical allowed in indoor air. The OSHA standard for TCE is higher than the EPA targets used for vapor intrusion, and while the DEQ environmental cleanup programs don't regulate the day-to-day operational emissions at a business, they do recommend that best management practices be used in the workplace setting to reduce operational TCE emissions to minimize potential health risks. In addition, for closure under risk-based rules which may require land-use restrictions, future exposure from TCE vapor intrusion may need to be evaluated to account for changes in use of the building or land use when OSHA standards no longer apply. For example, a property that is currently used for an active dry-cleaning business may be changed to residential or mixed use in the future when the dry-cleaning business is no longer in operation.

DWM recognizes that various EPA Regions and state/federal agencies have adopted a wide range of action levels regarding TCE in indoor air. At this time, DWM considers the USEPA TCE RfC published on IRIS to be health protective with respect to cardiac developmental effects. DMW's TCE action level response aligns with current recommendations from USEPA Region 4. DWM will continue to monitor recommendations from USEPA and other state/federal agencies and update this guidance to reflect relevant developments in the future.

Notification

State-Lead Programs:

When independent contractors working under DWM State-Lead programs receive analytical data indicating that women of child-bearing age may be exposed to TCE concentrations above the action level, they must notify the applicable DWM program they are working for within 1 business day of receipt of the data from the laboratory.

DWM Programs that are not State-Lead:

When remediating parties or Brownfields Program applicants and/or their environmental consultants receive analytical data indicating that women of child-bearing age may be exposed to TCE concentrations above the action level, the client (if applicable) and DWM must be contacted within 1 business day of receipt of the data from the laboratory. The client may notify DWM directly or instruct

the environmental consultant to do so. The environmental consultant should make clients aware of the reporting requirement.

Closed Sites:
DWM is currently evaluating and implementing plans to review and screen closed sites with known TCE contamination to identify ongoing exposures of concern, focused on the particular risks of TCE and the vapor intrusion pathway. Property owners and/or potentially responsible parties of previously closed TCE sites should not wait for DWM to make the initial contact. DWM encourages parties to review existing information about a site and begin to evaluate current conditions to determine if there is a potential for ongoing exposure to TCE. Parties should notify DWM if closed sites are discovered to have a potential for TCE. Updates on the progress of TCE closed sites review will be posted as they become available.

Sampling Considerations

DWM recommends time-integrated air sampling methods to account for temporal variability in vapor intrusion. Time-integrated samples provide a direct measurement of the average TCE concentration over a fixed period of time (e.g., 8 hours, 24 hours, 3 days, 7 days, etc.), which should be compared to the DWM action levels in Table 1. TCE concentrations are to be quantified using USEPA-approved volatile organic laboratory analytical methods. The time-integrated sampling periods should be chosen to enable identification of peak exposures that may exceed the applicable action level.

Response Actions

Since the exposure duration of concern for developmental effects is short, DWM will work with responding parties to identify appropriate mitigation options and begin implementation quickly for locations where women of child-bearing age are present. Women of child-bearing age should not be reintroduced to the contaminated area until laboratory data for two consecutive sampling events collected after temporary or permanent mitigation shows that TCE levels are below action levels.

Initial response actions that should be implemented immediately (typically within 24 hours) include:

- Risk communication with the potentially-at-risk population should be made by a toxicologist, health professional, human health risk assessor or qualified DWM personnel knowledgeable of the potential TCE health effects. A DWM risk assessor will be consulted by the DWM program with oversight. The DWM risk assessor can assist parties in providing health risk information to potentially affected individuals.
- Ensure appropriate fact sheets are provided to potentially affected individuals. (see links below).
- Vent the basement (if a basement exists in the building) or lowest level of the building by opening windows.
- Seal potential conduits where vapors may be entering the bottom floor of the building and any subsurface walls.
- Enclose and passively vent sumps.

Response actions that should be implemented <u>as soon as possible</u>, but which may require several days to two weeks to implement include:

- Adjust the building's pressurization (over-pressurize) by utilizing the HVAC system.
- Install carbon filtration on the HVAC system.
- Utilize portable air-purifying units in the building.

Response actions that should be implemented <u>as soon as possible</u>, but which may require several weeks to two months to design, install and test include:

- Installation of a sub-slab depressurization system.
- Installation of a soil vapor extraction system.
- Installation of new HVAC equipment to over-pressurize the building or bottom floor.

<u>Links to TCE factsheets including medical follow-up factsheets for primary care physicians:</u>

- DWM's *Frequently Asked Questions about Trichloroethylene (TCE) in Residential Indoor Air,* (insert web link)

- DWM's *Frequently Asked Questions about Trichloroethylene (TCE) in Workplace Indoor Air* (insert web link)

- NC DPH's *Trichloroethylene (TCE)* and *Trichloroethylene (TCE) Information of Health Professionals (*http://epi.publichealth.nc.gov/oee/az.html#tce

- ATSDR's *TCE ToxFAQs, TCE ToxGuide and Toxicological Profile for Trichloroethylene (TCE),* available at: **http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=30**

References:

ATSDR (Agency for Toxic Substances & Disease Registry). *Toxic Substances Portal Trichloroethylene (TCE), CAS ID #: 79-01-6*. Agency for Toxic Substances and Disease Registry, 4770 Buford Hwy NE, Atlanta, GA 30341. http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=30

DWM 2014. *Vapor Intrusion Guidance*. Division of Waste Management, Department of Environmental Quality.

MassDEP (Massachusetts Department of Environmental Protection). 2014. *Fact Sheet – TCE Toxicity Information: Implications for Chronic and Shorter-Term Exposure*.

MassDEP (Massachusetts Department of Environmental Protection). 2014. *USEPA Trichloroethylene Toxicity Values and Office of Research and Standards Recommendations Regarding Remediation Targets and Timeframes to Address Potential Developmental Risks*.

USEPA (United States Environmental Protection Agency). 2011. *Toxicological Review of Trichloroethylene (CAS No. 79-01-6) In Support of Summary Information on the Integrated Risk Information System (IRIS).* EPA/635/R-09/011F.

USEPA (United States Environmental Protection Agency). 2014a*. Memorandum – EPA Region 9 Interim Action Levels and Response Recommendations to Address Potential Developmental Hazards Arising from Inhalation Exposures to TCE in Indoor Air from Vapor Intrusion*. Region 9, San Francisco, CA.

USEPA (United States Environmental Protection Agency). 2014b. *Memorandum – Compilation of Information Relating to Early/Interim Actions at Superfund Sites and the TCE IRIS Assessment*. To Superfund Division Directors, EPA Regions 1 – 10, from Office of Superfund Remediation and Technology Innovation (OSRTI). August 27, 2014.

Frequently Asked Questions about Trichloroethylene (TCE) in Residential Indoor Air

May 2016

Why am I receiving this notice?

You are receiving this information because trichloroethylene (also called trichloroethene or "TCE") has been measured in the air in your home at a level which exceeds the Division of Waste Management's (DWM) action level concentration. When an indoor air concentration greater than the action level is identified, DWM requires immediate action be taken to reduce or eliminate the exposure to TCE in indoor air to prevent short-term exposures that pose a potential health risk to persons that may be sensitive to the effects of TCE.

- A TCE concentration above 2.1 micrograms per cubic meter of air ($\mu g/m^3$) is the DWM action level for women exposed in their homes and who are or may be in the first trimester of pregnancy. The health concern with breathing TCE above the action level is to the developing fetus.
- When a woman who is or may be in the first trimester of a pregnancy may be exposed to TCE above the action level concentration, immediate steps should be taken to promptly reduce the risk to the developing fetus. Developmental effects will not necessarily occur at exposures above the action level, but they cannot be ruled out and steps to address the potential risk are required.

What is TCE? How might I be exposed?

TCE is a man-made, colorless liquid used mainly as a solvent to remove grease from metal parts. It has also been an ingredient in some consumer products such as glues and paint removers. When TCE is released to soil or groundwater as a result of spills or leaks at a facility, it can evaporate and enter into a building's indoor air through seams and cracks in building foundations. This process is called "vapor intrusion."

What is the safe level of TCE in a home?

The United States Environmental Protection Agency (US EPA) recommends an indoor air guideline for residential settings of 2.1 $\mu g/m^3$. At or below this level there are no indications of a significant risk of adverse health effects.

What are the possible health effects from indoor air TCE exposure?

The possible health effects from breathing TCE depends on the concentration in indoor air, the length of the exposure, and whether and when a pregnant woman is exposed. Women who are in the first trimester of pregnancy are most sensitive to TCE exposures. This exposure period is of special concern because a woman may not yet know that she is pregnant. TCE exposures may increase the risk of heart malformations in the developing fetus. Breathing TCE over a long period of time may affect the immune system and increase susceptibility to infections. Long-term exposures may increase an individual's risk of cancers of the kidney, liver and non-Hodgkin's lymphoma.

What should I know about TCE if I might be pregnant?

Because TCE exposure during the first trimester of pregnancy could affect fetal heart development, pregnant women are of special concern. Where residential indoor air TCE concentrations exceed 2.1 µg/m3, DWM requires immediate notification of all women that may be exposed and that are of "child-bearing age" and immediate action to reduce or eliminate the exposure concentrations to below these levels. .

For exposures during the first trimester of pregnancy, DWM recommends the following protective measures:

- At TCE levels above the 2.1 $\mu g/m^3$ action level, women who may be in the first trimester of pregnancy and are concerned about their risk should consult with their physician and/or an occupational doctor familiar with chemical exposures. Depending on their specific exposure situation, they may want to

limit exposure while efforts to reduce the concentration of TCE are underway, for example by avoiding areas with TCE concentrations higher than the 2.1 µg/m^3 if possible, or by improving ventilation. TCE exposure concentrations above the action level may present a lower risk to the pregnant woman, but levels above this range must ultimately be reduced to meet US EPA and DWM's indoor air guideline in situations where women of child-bearing age may be exposed.

For exposures before or after the first trimester of pregnancy:

Exposures that end two to four weeks or more before a pregnancy are not indicated to contribute to an elevated level of risk since most TCE is eliminated from the body within that period.

What measures might be taken to reduce indoor air TCE levels??

Parties responsible for the contamination should are required to contract environmental professionals to quickly take steps to reduce the indoor air levels. The first mitigation steps usually include sealing sumps and foundation cracks and increasing ventilation. Portable carbon filtration systems and changes to the heating and ventilation system to increase the proportion of clean air into the home may also help to temporarily reduce concentrations while more permanent measures are being designed and implemented. Installing a sub-slab depressurization (SSD) system can be an effective measure in the longer term. An SSD system, which is similar to a radon abatement system, is a series of pipes under the basement with a fan that vents vapors to the outdoors. Groundwater treatment or soil vapor extraction may also be employed to reduce the source of TCE contamination.

What should I do if I'm concerned that my health has been affected?

If you have concerns about your health status, you should talk to your family doctor and/or an occupational doctor familiar with chemical exposures. When you meet with them, provide a copy of your TCE sampling results and the N.C. Division of Public Health's factsheet, *Trichloroethylene (TCE) Information for Health Professionals*, available at http://epi.publichealth.nc.gov/oee/az.html#tce

Where can my physician and I get more information about potential TCE health effects?

More information on TCE health effects and the basis of DWM's action levels can be found on DWM's website at http://epi.publichealth.nc.gov/oee/az.html#tce and the Agency for Toxic Substances and Disease Registry's (ATSDR) website at http://www.atsdr.cdc.gov/. Your physician may also contact the N.C. Division of Public Health's Occupational and Environmental Epidemiology Branch in Raleigh to speak with physicians familiar with chemical exposures (telephone 919-707-5900).

Where can I get more information about TCE contamination and cleanup?

More information DWM's guidance for sites with TCE contamination can be found at (http://epi.publichealth.nc.gov/oee/az.html#tce)

More information on the health effects associated with TCE exposures is available on the Agency for Toxic Substances and Disease Registry's (ATSDR) website at http://www.atsdr.cdc.gov/.

Adapted from Massachusetts Department of Environmental Protection's 'Important Information on Trichloroehylene (TCE) in Residential Indoor Air'.

Frequently Asked Questions about Trichloroethylene (TCE) in Workplace Indoor Air

May 2016

The purpose of this fact sheet is to provide information on trichloroethylene (also known as "TCE" or trichloroethene) workplace exposures due to hazardous waste sites as the source of contamination and worker exposure through breathing contaminated air in the workplace. This information applies to workplaces that do not utilize TCE as part of its operations. OSHA standards cover workplaces that utilize TCE as part of its operations.

Why am I receiving this notice?

You are receiving this information because TCE has been measured in the air in your workplace at a level which exceeds DWM's action level concentration for inhalation exposures. DWM has determined that when the inhalation exposure action level concentration is exceeded and persons that may be particularly sensitive to TCE exposures at these concentrations may be exposed immediate actions must be taken to reduce the exposure to below the action level concentration as quickly as possible. The population at risk at the action level concentration are women that maybe in their first trimester of a pregnancy, a period when a woman may not yet realize that she is pregnant. The potential health risks are permanent developmental effects manifested as damage to the developing heart of the unborn child (fetus).

- The DWM TCE action level for workplace (non-residential) inhalation exposures is 8.8 micrograms per cubic meter ($\mu g/m^3$) for women who are or may be in the first trimester of pregnancy.
- Immediate action to reduce the workplace air concentration to below the TCE action level is required to reduce the risk to the developing fetus. Developmental effects will not necessarily occur at exposures above this level, but they cannot be ruled out and steps to address the potential risk are required.
- Women exposed to TCE concentrations above the inhalation action level should wait 3 to 4 weeks after their exposures reach concentrations below the action level before getting pregnant to allow the TCE to be removed from your body. Contacting your personal physician to discuss your TCE exposure is recommended.

What is TCE? How might I be exposed?

TCE is a man-made, colorless liquid used mainly as a solvent to remove grease from metal parts. It has also been an ingredient in some consumer products such as glues and paint removers. When TCE is released to soil or groundwater as a result of spills or leaks at a facility, it can evaporate and enter into a building's indoor air through seams and cracks in building foundations. This process is called "vapor intrusion."

What is the safe level of TCE in the workplace?

The indoor air guideline for workplace settings is 8.8 $\mu g/m^3$. This value is based on the United States Environmental Protection Agency's (EPA's) guideline for continuous exposure, which has been adopted by DWM. The value is based on a cautious interpretation of the data. At or below this level, significant health effects are not indicated.

What are the possible health effects from indoor air TCE exposure?

The possible health effects from breathing TCE depend on the levels in indoor air, the length of exposure, and whether and when a pregnant woman is exposed. Women who are in the first trimester of pregnancy are most sensitive to TCE exposures. TCE exposures may increase the risk of heart malformations in the developing fetus. Breathing TCE over a long period of time may affect the immune system and increase susceptibility to infections. Long-term exposures may increase an individual's risk of cancers of the kidney, liver and non-Hodgkin's lymphoma.

What should I know if I might be pregnant?
Because TCE exposure during the first trimester of pregnancy could affect fetal heart development, pregnant women are of special concern. Where workplace indoor air TCE concentrations exceed 8.8 µg/m^3, DWM requires immediate notification to workers and actions to reduce concentrations to below 8.8 µg/m^3, or if feasible, eliminate the exposures.

For exposures during the first trimester of pregnancy, DWM recommends the following protective measures:

- At TCE levels above 8.8 µg/m^3, women who may be in the first trimester of pregnancy and are concerned about their risk may want to consult with their physician and/or an occupational doctor familiar with chemical exposures. Depending on the specific situation, there may be ways to minimize or eliminate the risk, for example by avoiding areas of the workplace with higher TCE levels if possible. TCE levels below 8.8 µg/m^3 present a lower risk to the pregnant woman. Levels above this range must ultimately be reduced to meet EPA and DWM's indoor air guidelines.

For exposures before or after the first trimester of pregnancy:

- Exposures that end two to four weeks or more before a pregnancy are not indicated to contribute to an elevated level of risk since most TCE is eliminated from the body within that period.

What measures might be taken to reduce TCE levels in my workplace?
Parties responsible for the contamination are required to contract environmental professionals to quickly take steps to reduce the indoor air levels. The first mitigation steps usually include sealing sumps and foundation cracks and increasing ventilation. Portable carbon filtration systems and changes to the heating and ventilation system may also help to temporarily reduce concentrations while more permanent measures are being designed and implemented. Installing a sub-slab depressurization (SSD) system can be an effective measure in the longer term. An SSD system, which is similar to a radon abatement system, is a series of pipes under the basement with a fan that vents vapors to the outdoors. Groundwater treatment or soil vapor extraction may also be employed to reduce the source of TCE contamination.

What should I do if I'm concerned that my health has been affected?
If you have concerns about your health status, you should talk to your family doctor and/or an occupational doctor familiar with chemical exposures. When you meet with them, provide a copy of your TCE sampling results and the N.C. Division of Public Health's factsheet, *Trichloroethylene (TCE) Information for Health Professionals*, available at http://epi.publichealth.nc.gov/oee/az.html#tce.

Where can my physician and I get more information about potential TCE health effects?
More information on TCE health effects and the basis of DWM's action levels can be found on DWM's website at http://epi.publichealth.nc.gov/oee/az.html#tce and the Agency for Toxic Substances and Disease Registry's (ATSDR) website at http://www.atsdr.cdc.gov/. Your physician may also contact the N.C. Division of Public Health's Occupational and Environmental Epidemiology Branch in Raleigh to speak with physicians familiar with chemical exposures (telephone 919-707-5900).

Where can I get more information on TCE contamination and cleanup?
More information on DWM's guidance for sites with TCE contamination can be found at http://epi.publichealth.nc.gov/oee/az.html#tce. More information on the health effects associated with TCE exposures is available on the Agency for Toxic Substances and Disease Registry's (ATSDR) website at http://www.atsdr.cdc.gov/.

Adapted from Massachusetts Department of Environmental Protection's 'Important Information on Trichloroethylene (TCE) in Workplace Indoor Air'.

Time Line of Trichloroethylene (TCE) Inhalation Action Level Toxicity References and Discussion Documents
N.C. Department of Environmental Quality
January 2017

2016, Apr., Trichloroethylene (TCE) Indoor Air Inhalation Immediate Action Levels and Response (Draft), NC DEQ DWM

2016, Aug., Makris et al., *A Systemic Evaluation of the Potential Effects of Trichloroethylene Exposure on Cardiac Development*. Reproductive Toxicology. 2016, 65:321-358. http://dx.doi.org/10.1016/j.reprotox.2016.08.014. [1]

2016, Jan., Wirbisky et al., *Mitochondrial Dysfunction, Disruption of F -Actin Polymerization, and Transcriptomic Alterations in Zebrafish Larvae Exposed to Trichloroethylene*. Chem. Res. Toxicol. 2016, 29, 169−179 [2]

2015, Mar., *Disruption of Cardiogenesis in Human Embryonic Stem Cells Exposed to Trichloroethylene*. Jiang et al. Environmental Toxicology DOI: 10.1002/tox.22142, Wiley Online Library [3]

2014, *Chapter 8, Environmental Sensitivity to Trichloroethylene (TCE) in the Developing Heart*, Ornella I. Selmin, Om Makwana, and Raymond B. Runyan. In *Trichloroethylene*: *Toxicity and Health Risks*, Kathleen M. Gilbert, Sarah J. Blossom Editors, Humana Press Molecular and Integrative Toxicology Series [4]

2014, Nov., *Maternal Residential Proximity to Chlorinated Solvent Emissions and Birth Defects in Offspring: A Case–Control Study*. Brender et al. Environmental Health 2014, 13:96 [5]

2014, Oct., *Draft Toxicological Profile for Trichloroethylene*, ATSDR, U.S. DHHS [includes discussions of human exposures resulting in fetal cardiac effects] [6,7,8]

2014, Aug., *Review and Recommendations for TCE Short-Term Action Levels in Indoor Air*, TRC Inc., http://www.trcsolutions.com/

2014, July, *EPA Region 9 Response Action Levels and Recommendations to Address Near-Term Inhalation Exposures to TCE in Air from Subsurface Vapor Intrusion*, U.S. EPA Region 9

2014, Mar., *Assessing the Congenital Cardiac Toxicity of Trichloroethylene: Key Scientific Issues*. Massachusetts Department of Environmental Protection Office of Research and Standards

2013, Mar., Makwana et al., *Low Dose Trichloroethylene Alters Cytochrome P450 - 2C Subfamily Expression in the Developing Chick Heart*. Cardiovasc Toxicol. 2013 March; 13(1): 77–84 [9]

2013, Feb., *Health Consultation, Millsboro TCE, Millsboro, Delaware*. U.S. DHHS, (ATSDR) Agency for Toxic Substances and Disease Registry.

2011 Sept., *Toxicological Review of Trichloroethylene*, IRIS, U.S. EPA [source of non-cancer RfD and RfC, and cancer potency values]

2003, Mar., Johnson et al., *Threshold of Trichloroethylene Contamination in Maternal Drinking Waters Affecting Fetal Heart Development in the Rat*. Environ Health Perspect. 111:289-292. [IRIS RfD / RfC critical effect study for fetal cardiac malformations]

[1] The U.S. EPA performed an updated literature search of TCE-related developmental cardiac defects and developed a putative adverse outcome pathway (AOP) construct to explore key events for the most commonly observed cardiac dysmorphologies, particularly those involved with epithelial-mesenchymal transition (EMT) of endothelial origin (EndMT). They concluded: "*A hypothesis-driven weight-of-evidence analysis of epidemiological, toxicological, in vitro, in ovo, and mechanistic/AOP data concluded that TCE has the potential to cause cardiac defects in humans when exposure occurs at sufficient doses during a sensitive window of fetal development. The study by Johnson et al. (2003) was reaffirmed as suitable for hazard characterization and reference value derivation, though acknowledging study limitations and uncertainties*."

[2] A laboratory study exposing zebrafish embryos to TCE identified mechanisms of cardiovascular toxicity associated with adverse developmental effects (zebrafish possess developmental genomic cardiovascular similarities to humans and are a common model for cardiac development). Observed TCE dose-response-related effects included loss of the vasculature network assembly, decreases in the development of new blood vessels (angiogenesis) and actin fibers, and mitochondrial function. These observations support human fetal cardiac malformation as the critical effect during early embryonic development. The heart is the first organ developed during embryogenesis and a competent vascular network is required for endothelial cell differentiation, proliferation and migration. Gene expression alterations to 70 genes associated with cardiovascular disease, organ morphology and function, cancer, liver and digestive system development and function, and kidney toxicity, and skeletal and muscular disorders were observed. In addition, TCE-induced abnormalities were observed to genes associated with cellular growth and proliferation, cell-to-cell signaling and cell cycle control, all of which are critical pathway components associated with tumor morphology and regulation. Significant effects were observed at the lowest test concentration, 10 ppb TCE.

[3] Cardiac function and development-associated gene expression levels were significantly altered in a human embryonic stem cell cardiac differentiation model. Species-specific inhibitory effects of TCE on heart development associated with the inhibition of human stem cell differentiation to cardiac muscle cells were reported. Significant interference with cardiac muscle cell Ca^{2+} (calcium) channel pathways were also observed and are implicated in TCE impacts to cardiac differentiation during early embryonic organogenesis, as well as subsequent cardiotoxicity and abnormal cardiac morphology.

[4] This review of the current-science of TCE toxicity includes the referenced chapter which discusses the observation of a non-monotonic dose-response (the response decreases with increasing dose) of TCE effects at environmentally-relevant concentrations observed in other studies. Significantly increased effects were seen on gene expression and cardiac function at exposure concentrations just above the TCE MCL (5 ppb). Examination of early heart valve development indicated that formation of valve progenitors were impaired. Changes in the expression of several genes involved in muscle cell calcium homeostasis and myocardial contraction were implicated. Calcium-mediated contraction in the heart was impaired and corresponded to changes in intracellular calcium flux and cardiac output. The non-monotonic dose-response characteristic reported in some studies was linked to the expression of a specific phase I metabolic enzyme (cytochrome P450 CYP2C) prior to the later development of the liver's phase I metabolic response capacity. Low doses of TCE were metabolized in the embryonic chick heart model by the localized CYP2C metabolizing enzyme family, providing a mechanism of early TCE and TCE metabolite-associated toxicity in the developing heart prior to the development of the liver and its ability to provide metabolizing enzyme systems in response to toxic insults in the embryo and fetus.

[5] A population-based case-control epidemiological study of the Texas Birth Defects Registry for births occurring during 1996-2008 examined the relationship between maternal residential proximity to industrial releases of chlorinated solvents and selected birth defects. The Texas database included >60k cases and >244k controls. Exposures were estimated using distance from the source and reported annual amounts of solvent releases (EPA TRI data). Logistic regression indicated a significant association of TCE exposure and obstructive heart defects in

offspring of mothers 35 years or older (odds ratio 1.43, 95% CI 1.08, 1.88; the odds ratio represents the odds of an exposed person developing the disease relative to a non-exposed person developing the disease). Other TCE and maternal proximity to emission-related associations identified in the Texas study included maternal age-related effects associated with oral cleft defects and the likelihood of any type of heart defect or septal heart defect, as well as an increased likelihood of spina bifida in the offspring of mothers of any age.

[6] A study of an Endicott NY residential population exposed via vapor intrusion. Findings included a significantly elevated risk of cardiac defects at birth. Total cardiac defects at birth were twice as prevalent as expected. A 2.5-fold increase in the rate of congenital heart disease in children was reported for parents exposed in drinking water during the month before conception and the 1st trimester of pregnancy.

[7] Milwaukee, WI residential exposures to TCE resulted in significant (3-fold) increased risk of congenital heart defects in children born to women living within 1.3-miles of a TCE-emitting site (as compared to those living outside the 1.3-mile range).

[8] ATSDR states, when discussing the Johnson et al. 2003 study, that "…*However, in the absence of convincing information to the contrary, the report of trichloroethylene-induced cardiac malformations in rat fetuses is considered valid and relevant to humans. The increased incidences of fetuses with cardiac malformations from the rat dams administered trichloroethylene during gestation serve as partial basis for the chronic-duration inhalation and oral MRLs for trichloroethylene*…", and they later state "…*EPA concluded that "while the Johnson et al. studies have limitations, there is insufficient reason to dismiss their findings, especially when the findings are analyzed in combination with the remaining body of human, animal and mechanistic evidence*".

[9] This study demonstrates that the earliest embryonic expression of phase I detoxification enzymes is in the developing heart. The expression of these enzymes is relevant to the unique susceptibility of the embryonic heart at the earliest stages of development to environmental teratogens, including TCE. Developing chick embryos were dosed with TCE at 8 and 800 ppb, followed by examination of genetic material-associated effects in cardiac and other tissues. The study reported TCE-induced adverse effects to cardiovascular development prior to development of the liver systems able to mediate xenobiotic insults. Increased expression of early embryo cardiac tissue-specific cytochrome P450 metabolizing enzyme genetic material (mRNA and cytochrome precursor proteins) were observed, with no detectable response in extra-cardiac tissue. In this study, the dose-response in the cardiac tissue was non-monotonic (the response was greater at 8 ppb TCE than at 800 ppb TCE), supporting observations in prior studies. A known cytochrome oxidative metabolite of TCE is trichloroacetic acid (TCA), which has been shown to elicit greater cardiac toxicity than TCE. One possible pathway of the non-monotonic dose-response is that in early stages of embryonic TCE exposures, the cardiac-specific enzyme system metabolizes TCE, producing toxic metabolites, that act in concert with the TCE to induce adverse cardiac effects. As exposure concentrations increase, response systems may be quickly overwhelmed, until additional metabolizing systems are developed in the liver and other tissues, producing toxic metabolites that increase the level of adverse effects.

Summary of Other State and Federal TCE Action Levels (October 2016)

Agency	Date	Residential Action Levels	Commercial/ Industrial Action Levels	Residential Screening Levels	Commercial/ Industrial Screening Levels
EPA Region 9	2014	2.0	8.0		
California EPA	2014	2.0	8.0	0.48	0.48
Connecticut DPH & DEEP	2015	5.0	8.0	2.0	2.0
New Hampshire DES	2013	2.0	8.8	0.4	1.8
North Carolina DEQ	2016	2.1	8.8	0.417	1.75
Wisconsin DNR	2015	2.1	8.8		
EPA Region 9	2012	15.0	15.0		
New Jersey DEP	2013	4.0	18.0	3.0	3.0
New York State DOH & DEC	2015	20.0	20.0	2.0	2.0
EPA Region 9	2014	6.0	24.0		
California EPA	2014	6.0	24.0	0.48	0.48
Massachusetts DEP	2014	6.0	24.0	2.0	8.0
Massachusetts DEP	2014	20.0	60.0		
Indiana DEM	2016	20.0	290.0	2.1	8.8
Oregon DEQ	2010	47.0	290.0	0.47	2.9
Michigan DEQ	2013			2.1	8.8
Minnesota DH & PCA	2016			2.0	6.0
EPA Region 10	2012			2.0	8.4
Alaska DEC	2014			2.0	8.4
Washington DOE	2016			2.0	2.0
Kansas DHE	2015			2.09	2.09
US EPA	2016			2.1	8.8
Montana DEQ	2011			2.1	8.8
Ohio EPA	2016			2.1	8.8
California OEHHA	2012			2.5	2.5
Missouri DNR	2006			12.8	27.3
Pennsylvania DEP	2004			12.0	48.0
ATSDR	2012			21.0	190.0

Time Plot of Residential and Industrial Action Levels