Update for ATSDR Health Assessors

Including APPLETREE Partners

February 2021

Guidance & Clearance News

The purpose of this newsletter is to keep you informed about the guidance and resources that are available for use in your health evaluations.

What is in this Newsletter?

The following are topics included in this edition of the OCHHA ADS Newsletter. In 2021, the OCCHA ADS Office will provide health assessors an index of all topics covered in these newsletters from their inception.

Evaluating Carcinogens without CREGs

What follows is not meant to be comprehensive step-by-step guidance of the screening process for carcinogens, but rather an explanation of how to handle those carcinogens without Cancer Risk Evaluation Guides (CREGs). Please note that the following description of ATSDR's screening process assumes that the CREG or alternative cancer based non-ATSDR screening value (SV) is lower than the respective non-cancer comparison value (CV) for that chemical. Although this is true for most carcinogens, there are some exceptions where the non-cancer CV is lower than the CREG or alternative cancer-based SV. Please remember that ATSDR's screening process strives to select the most conservative CV or non-ATSDR SV that is health-protective and well-supported.

The OCHHA ADS Group will provide health assessors with a list of chemicals that are carcinogenic but do not have a CREG. This list will be posted on the PHAST Resources page. In addition, the ADS Group is exploring ways to alert health assessors within PHAST when a chemical is in this category. For chemicals determined to have carcinogenic properties, the first step in our screening is to compare the chemical/medium concentration against ATSDR CREGs. In most cases, CREGs are ATSDR comparison values calculated using EPA cancer slope

factors (CSFs) for oral exposures or EPA inhalation unit risk values (IURs) for inhalation exposures available from EPA's Integrated Risk Information System (IRIS).

What to do when a carcinogen has no CREG in PHAST?

Over 100 chemicals are classified as carcinogens (by at least one agency) but do not have ATSDR-generated CREG values in PHAST. Because ATSDR calculates CREGs in most cases from IRIS-based CSFs and IURs, carcinogens without CSFs or IURs will also not have CREG values. Based on ATSDR guidance, health assessors have two options. First, you can select the carcinogen as a contaminant of concern (CoC) for qualitative evaluation (see Step 2 below) or you could consider the following:

1. **Is an alternative cancer screening value and associated cancer potency value available from a different source?** Other sources include the EPA's Regional Screening Levels (RSLs) table and California Environmental Protection Agency (Cal EPA) OEHHA database at the following link, (https://oehha.ca.gov/chemicals). Consult your ADS about using a cancer screening value from EPA's RSL table, Cal EPA, or another agency. In the limitations section of your document, note the use of the other agency's value(s) (i.e., a non-ATSDR cancer SV), and describe the validity of the cancer potency value.

2. **If no potency value is available to calculate the cancer risk,** then discuss the carcinogen in a qualitative manner stating the cancer classification listed by National Toxicology Program (NTP), EPA, or other classifying agency. Over 100 chemicals have been classified as a carcinogen but do not have a cancer potency value making numerical estimates of cancer risk not possible. Because of this uncertainty, you may want to make recommendations to stop, prevent, or reduce exposure. Consider the following in a qualitative discussion:

   - Mode of action
   - Weight-of-evidence
   - Dose-response assessment

   Include in your document whether there are other chemical drivers in the same pathway that require recommendations to protect public health. Reducing or stopping exposure from these other chemicals may also protect from exposure to the carcinogen. In the limitations section of your document, note this qualitative chemical evaluation and include the cancer classification from other groups. State how your evaluation impacts the strength and certainty of your conclusion.

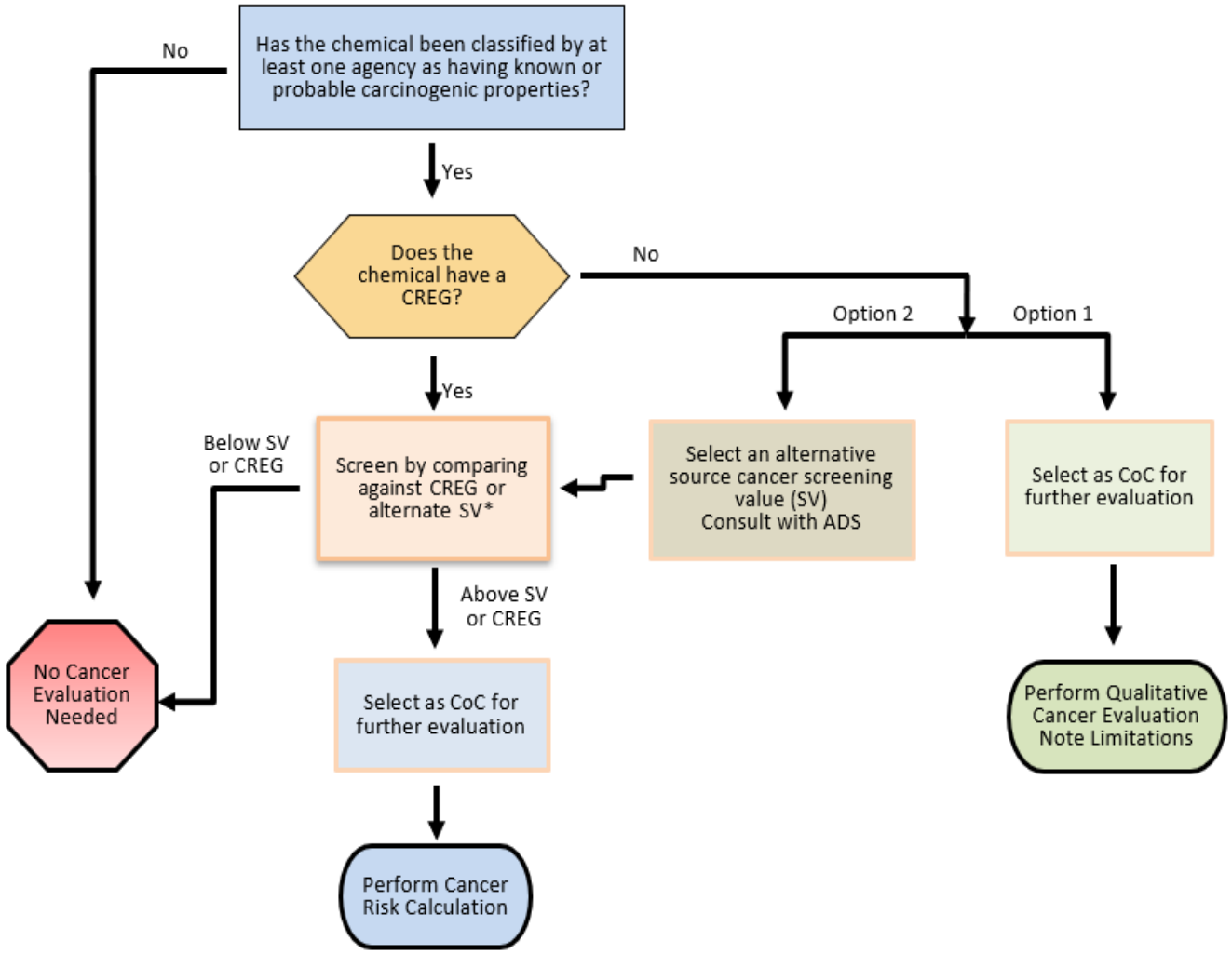
3. **Why would EPA's IRIS have chemicals classified as being carcinogenic, but have no cancer potency value, such as a CSF or IUR?** When developing cancer toxicity values, EPA considers the following factors that influence confidence in the numerical cancer risk estimate (confidence in quantitation):

   - Appropriateness of data for estimating human carcinogenic risk
   - Quality of study design
   - Strength of study results

- Appropriateness of model application to the data
- Support of risk estimate by data from collateral studies
- Evolving science

Therefore, data limitations may prevent EPA from deriving a CSF or IUR. In some cases, EPA may have derived a cancer toxicity value, but withdrew the value from IRIS because new data cast doubt on the previously derived value. Thus, not all chemicals classified by EPA will have a cancer toxicity value.

Flowchart for Evaluating Carcinogens with no CREGs



*Please note that the instructions in this box assumes that the CREG or alternative cancer-based SV is less than its respective non-cancer ATSDR CV or non-cancer alternative SV. Health assessors should follow the ATSDR screening process as described in the Public Health Assessment Guidance Manual to choose the lowest CV or SV that is health protective and well-supported.

Flow Chart Description

Title: "Flowchart for Evaluating Carcinogens with no CREGs"

Top of chart begins with question: "Has the chemical been classified by at least one agency as having known or probable carcinogenic properties?"

If the answer is “No”, then no cancer evaluation needed

If the answer is “Yes”, then ask “Does the chemical have a CREG?”

If the answer is “No”, then there are two options

Option 1 is to select as a CoC for further evaluation to perform a qualitative cancer evaluation and to note limitations

Option 2 is to select an alternative source cancer screening value (SV) and to consult with ADS

For both Option 2 and if the answer to the question “Does the chemical have a CREG?” is “Yes”, then screen by comparing against the CREG or alternate SV. Please note that this instruction assumes that the CREG or alternative cancer-based SV is less than its respective non-cancer ATSDR CV or non-cancer alternative SV. Health assessors should follow the ATSDR screening process as described in the Public Health Assessment Guidance Manual to choose the lowest CV or SV that is health protective and well-supported.

If below the SV or CREG, then no cancer evaluation is needed.

If above SV or CREG, then select as CoC for further evaluation and perform cancer risk calculation

PHAST V1.8 Updates

ATSDR continues to enhance PHAST with the newest version (v1.8) released on February 12, 2021. What follows is a summary of the enhancements in PHAST v1.8.

1. Health Guideline Information: When you search for a chemical, a dropdown menu appears where you select the chemical. This dropdown menu now has information about whether comparison values (CVs) and health guidelines are available and whether either a CSF or IUR is available. An example is shown below. This is particularly useful for chemicals with multiple forms (e.g., PCBs or chromium) where health guideline and cancer toxicity values are available for some forms but not others.

CASRN	Contaminant Name	Standard Name	CV/HG	Cancer Risk
7440-43-9	Cadmium	Cadmium	Oral/Inhalation	IUR

2. Occupational Tenure: Using information from several sources, such as the Bureau of Labor Statistics, default occupational exposure durations were changed to reflect the current workforce (20 years for reasonable maximum exposure (RME); 5 years for central tendency estimate (CTE); and 3.1 years for part-time) (BLS 2019, BLS 2018, Copeland 2019, U.S. EPA 2001). These new values can be found in the 2020 Guidance for Inhalation Exposure (aka the Air EDG) (ATSDR 2020). Other Exposure Dose Guidance (EDG) documents that have occupational tenure information, such as the Drinking Water EDG and the Soil Ingestion EDG, are being updated (ATSDR 2016, 2018).

3. Health Guideline Module reformatted: The tables summarizing the critical studies used to derive the Minimal Risk Level (MRL), Reference Dose (RfD), and Reference Concentration (RfC) have been reformatted so that it's easier to read the study health effects. A sample is shown below.[1]

Oral Health Guideline Information

Species	No./Group	Doses	Exposure Parameters	Target System	Study Effect		Uncertainty Factor (Total)
					Type	Level	
ATSDR Chronic MRL: 0.0003 mg/kg/day							
Human				Dermal, Vascular, Liver	NOAEL	0.0008 mg/kg/day	3

Study Health Effects

The chronic oral MRL is based on a human study resulting from ingestion of contaminated drinking water. Tseng et al. estimated a NOAEL of 0.8 µg As/kg/day and a dermal LOAEL of 14 µg As/kg/day that showed hyperkeratosis, especially on the palms and soles, as well as hyperpigmentation of the skin. Several other dermal LOAELs have been identified between 1.4 to 15 µg As/kg/day. The MRL worksheet states, "Collectively, these [dermal] studies indicate that the threshold dose for hyperpigmentation and hyperkeratosis is approximately 0.002 mg As/kg/day."

Other possible effects at or near these dermal LOAELs include an enlarged liver, bronchitis, gastrointestinal effects, and peripheral vascular effects, such as cyanosis, gangrene, and, in the Taiwanese populations, the condition known as "Blackfoot Disease".

For dermal effects, health assessors should compare site-specific doses to the threshold of 2 µg As/kg/day. Health assessors also should review the LSE figures and tables in the tox profile for health effects to other organ systems at similar doses.

Citation(s)

Tseng, WP, Chu HM, How SW, et al. 1968. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. J Natl Cancer Inst 40:453-463. Tseng, WP. 1977. Effects and dose-response relationships of cancer and Blackfoot disease with arsenic. Environ Health Perspect 19:109-119.

[1] Levels of significant exposure (LSE), no observed adverse effect level (NOAEL), lowest observed adverse effect level (LOAEL)

4. Input Parameter Tables: When exporting results tables to Word, you also have the option to export the default exposure parameters tables. These tables are now 508-compliant when exported and are shown below.

PHAST PUBLIC HEALTH ASSESSMENT SITE TOOL

Default Parameters Table
PHAST Report, v1.7.17.0, December 7, 2020

Default Exposure Factors

Duration Category	Days per Week	Weeks per Year	Years	Exposure Group Specific $EF_{noncancer}$	Exposure Group Specific* EF_{cancer}
Acute	-	-	-	1	NC
Intermediate	7	-	-	1	NC
Chronic	7	52.14	See exposure group specific exposure durations	1	$=EF_{noncancer}$ x Exposure Duration for Cancer $_{Exposure\ Group}$ (years) ÷ 78 years

Abbreviations: EF = exposure factor; NC = not calculated
* Cancer Risk is averaged over a lifetime of exposure (78 years).

Default Exposure Parameters

Exposure Group	Body Weight (kg)	CTE Exposure Duration for Cancer (years)	CTE Intake Rate (liters/day)	RME Exposure Duration for Cancer (years)	RME Intake Rate (liters/day)
Birth to < 1 year	7.8	1	0.504	1	1.113
1 to < 2 years	11.4	1	0.308	1	0.893
2 to < 6 years	17.4	4	0.376	4	0.977
6 to < 11 years	31.8	5	0.511	5	1.404
11 to < 16 years	56.8	1	0.637	5	1.976
16 to < 21 years	71.6	0	0.77	5	2.444
Total Child (all age groups)	-	12	-	21	-
Adult	80	12	1.227	33	3.092
Pregnant Women	73	-	0.872	-	2.589
Lactating Women	73	-	1.665	-	3.588

Abbreviations: CTE = central tendency exposure (typical); kg = kilograms; RME = reasonable maximum exposure (higher)

5. Vinyl Chloride: For vinyl chloride, EPA does not use the Age Dependent Adjustment Factor or ADAF to adjust cancer risk estimates. Instead, EPA has two sets of cancer toxicity values. One set is used when exposure starts during childhood while the other set is used when exposure starts during adulthood. This makes using the correct value tricky in PHAST. Just as a reminder for vinyl chloride, oral CSFs use either 0.72 $(mg/kg/day)^{-1}$ when exposure starts during adulthood or 1.4 $(mg/kg/day)^{-1}$ when exposure starts during childhood. Similarly, the IURs are 4.4E-6 $(\mu g/m^3)^{-1}$ (adulthood) or 8.8E-6 $(\mu g/m^3)^{-1}$ (childhood) (U.S. EPA 2021).

When you run the default scenario, PHAST will automatically use the childhood cancer toxicity value for children birth to < 21 years and will use the adulthood cancer toxicity value for adults exposed for 33 years. When children grow up in a house and continue to live there as adults, cancer risk is calculated differently. For this combined 21-years exposure as a child plus 12 years exposure as an adult at the same house, PHAST will use the childhood cancer toxicity value for both durations. If you add a custom group, PHAST will prompt you to designate the custom group as child or adult and will apply the appropriate cancer toxicity value. If you have questions or concerns, please contact PHAST@cdc.gov.

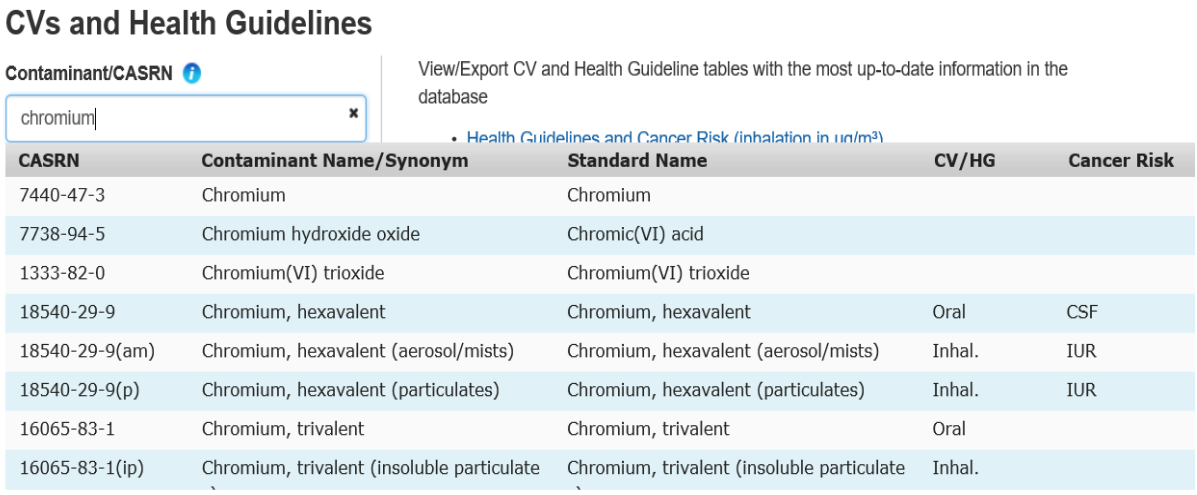
6. Dioxin: If you enter "dioxin" when selecting a chemical, 2,4,7,8-TCDD will be the first chemical in the dropdown list thus making it easier to find.

7. RfDs and RfCs: For chemicals where ATSDR does not have a chronic MRL, we default to using the RfD or RfC. However, we have identified some RfDs and RfCs that are greater than ATSDR's intermediate MRL. This means that the intermediate MRL is more health protective than the RfD or RfC. In those situations, we have disabled RfDs and RfCs from being used to calculate chronic HQs and disabled reference dose media evaluation guidelines (RMEGs) from being used in the CV screening. PHAST will still use the intermediate MRL to calculate intermediate HQs and use intermediate environmental media evaluation guides (EMEGs) in the CV screening. When evaluating non-cancer, you should use the intermediate MRL and not the RfD or RfC.

8. Chromium: Searching for Chromium Health Guidelines: When you enter chromium in the contaminant search field, the dropdown list of chemicals will show the 7 specific chromium contaminants at the top of the list. This will make it easier for you to find the most common forms of chromium without having to enter a specific chemical name or searching through a long list of synonyms. Of course, if you know you want a specific form, you can type that in the field (e.g., hexavalent chromium).

Remember, the dropdown list now includes information about whether health guidelines or cancer toxicity values are available for the different forms of chromium. This hopefully will prevent someone from selecting chromium, which has no health guidelines. It will also remind folks that health guideline information is available for other chromium forms.

Chromium Health Guidelines Revamped: Health guidelines and cancer toxicity values for chromium vary depending upon the chemical form. We have segregated this information in PHAST according to the chemical forms, which now show the availability of health guidelines and cancer toxicity values when users search on chromium:



CVs and Health Guidelines

Contaminant/CASRN

chromium

View/Export CV and Health Guideline tables with the most up-to-date information in the database

- Health Guidelines and Cancer Risk (inhalation in ug/m3)

CASRN	Contaminant Name/Synonym	Standard Name	CV/HG	Cancer Risk
7440-47-3	Chromium	Chromium		
7738-94-5	Chromium hydroxide oxide	Chromic(VI) acid		
1333-82-0	Chromium(VI) trioxide	Chromium(VI) trioxide		
18540-29-9	Chromium, hexavalent	Chromium, hexavalent	Oral	CSF
18540-29-9(am)	Chromium, hexavalent (aerosol/mists)	Chromium, hexavalent (aerosol/mists)	Inhal.	IUR
18540-29-9(p)	Chromium, hexavalent (particulates)	Chromium, hexavalent (particulates)	Inhal.	IUR
16065-83-1	Chromium, trivalent	Chromium, trivalent	Oral	
16065-83-1(ip)	Chromium, trivalent (insoluble particulate	Chromium, trivalent (insoluble particulate	Inhal.	

We made these changes based on comments we got that it was confusing to present inhalation and oral guidelines together because the health guidelines are specific to the chemical form of chromium. Please let us know what you think. If you have suggestions for improving how this information is presented, please send them to PHAST@cdc.gov.

Updates to the Guidance for Inhalation Exposures

ATSDR recently released Guidance for Inhalation Exposures, commonly called the Air EDG (ATSDR 2020). In version 1, Table 1 reported the default parameters for daycares and schools, such as CTE and RME times spent at school. As we coded PHAST to generate the Air Module, we realized that Table 1 presented some confusion because the exposure duration parameters for older children at daycare facilities (e.g., 5-year old) was different than 5-year old children in kindergarten. Therefore, we separated the two groups. Table 1 below shows the default parameters for children at daycare facilities, and Table 2 shows the default parameters for pre-kindergarten, kindergarten, and grade school children through the 12th grade. Version 2 of the guidance is now on the PHAST resource page.

Table 1. Children: time per day spent in childcare facilities

Age group	Daily CTE (hr/day)	Daily RME (hr/day)	Annual CTE (wks/yr)*	Annual RME (wks/yr)
Birth to <1 year	5.2	11.8	50	52.14
1 to <2 years	4.8	9.9	50	52.14
2 to <6 years	6.4	9.6	50	52.14

Table 2. Children: time per day spent in grade school pre-kindergarten through 12th grade

School Grade Level	Age (yrs)	Default School Placement	Daily (hr/day)		Annual (wks/year)	
			CTE	RME	CTE	RME
Pre-Kindergarten	3<5	Pre-Kindergarten	7.0	9.6	39	47
Kindergarten	5<6	Kindergarten	7.0	9.6	39	47
1st – 5th grades	6<11	Elementary	6.7	9.0	39	47
6th – 8th grades	11<14	Middle	6.7	9.3	39	47
9th – 12th grades	14<18	High	6.7	9.3	39	47

The good news is that the Air Module in PHAST will have options for you to select a daycare scenario as well as a school scenario. Grade schools can vary in how students are designated. Some school systems have junior high instead of middle school and the age of children in those two categories often differ. Therefore, PHAST will be coded with the flexibility to allow you to switch grades between categories. PHAST will offer training on how this is done when the air module is released, hopefully in Spring 2021. Eventually, the PHAST team will create similar daycare and school scenarios for the drinking water and soil ingestion pathways.

Lingering VOC (Volatile Organic Compound) Groundwater Plumes and VI (Vapor Intrusion)

VOC groundwater plumes, especially those with chlorinated VOCs, often persist for decades and are difficult to remediate. If occupied buildings are nearby, ATSDR recommends sampling the VI pathway (indoor air, subslab gas, and outdoor air) during cold and hot weather. The measured VOC levels are screened in each media using PHAST air and vapor intrusion screening values and assessed using ATSDR's guidance *Evaluating Vapor Intrusion Pathways* [ATSDR 2016]. Actions can be taken to reduce exposures in buildings with levels of concern. Other nearby buildings may have low indoor air concentrations because the building conditions were not favorable for VI to occur. However, if the contaminant source remains above VI CVs, there may be potential for VI to occur with changing building conditions.

ATSDR recommends continued periodic sampling when VOCs remain above VI CVs in the groundwater beneath or near occupied buildings, even if VI was not initially found to be a health concern. This continued sampling is recommended because VI into buildings can change over time due to aging or normal events, such as replacing a broken furnace or installing a sump pump to prevent basement flooding. As long as the source of contamination remains in place, vapor intrusion may become a concern.

A ubiquitous natural indicator, radon, can alert occupants to increased VI. Radon is a natural cancer-causing gas that comes from rock and soil and enters homes by similar routes as subsurface VOCs. Continuous radon monitors have recently become available to homeowners and occupants (around $200). If community members are monitoring radon before and after necessary building changes, they could detect a change in soil gases intruding into the building.[2] If there is a plan for periodic VOC sampling at the site, an increase in radon

[2] Note that a single elevated indoor radon level is not necessarily indicative of chemical VI, as that may result from an elevated radon source even with slow soil gas infiltration rates.

could be an indicator that resampling of VOCs is needed. Studies have found that sampling VOCs during episodes of highest radon levels improves the chances of detecting active vapor intrusion [Schuver 2019].

If health assessors are working on a VOC site and find community members that express an interest in doing their own radon monitoring, ATSDR has developed a plain language fact sheet template, *Home Alterations and Vapor Intrusion*, to help facilitate health education on this topic. The fact sheet is currently available in the PHAST Resource Section, but it will eventually be migrated to the online Public Health Assessment Guidance Manual (PHAGM) along with the following additional ATSDR vapor intrusion resources:

- Evaluating Vapor Intrusion Pathways [ATSDR 2016]
- VI Conceptual Site Model Figure [ATSDR 2019a]
- Vapor Intrusion Data Quality Evaluation Worksheet [ATSDR 2019b]

You may also contact the Vapor Intrusion Subject Matter Expert (SME), Tonia Burk, at fxt9@cdc.gov for assistance.

New ATSDR Completed or Evolving Guidance Documents and Where to Find Them

Do you know where to find all the latest ATSDR guidance documents?

The table below shows recently completed guidance and new guidance coming soon!

Guidance Topics	Status	Point(s) of Contact
Particulate Matter Guidance	Completed	Michelle Colledge; Greg Ulirsch
Exposure Point Guidance for Non-Discrete Sampling	Spring 2021	Greg Ulirsch; James Durant
Exposure Point Concentration (EPC) Guidance for PAHs	Winter 2021	Greg Ulirsch; James Durant
Exposure Unit (EU) Guidance	Completed	Greg Ulirsch; James Durant
Guidance for Inhalation Exposures	Completed	Michelle Colledge

All of the latest guidance documents are posted in the Resources Section in PHAST. In addition, all ADS Newsletters along with a list of current SMEs have been added to the Resources Section of PHAST. In the future when the online PHAGM is launched, all guidance (including these newsletters) will be housed there.

Only specific PHAST-related guidance and supporting materials will remain within the Resources Section in PHAST. Look for updates from the ADS Office in 2021 about the launch of the updated PHAGM. In addition, the OCHHA ADS Office is currently updating several outdated guidance documents and hope to have those released in 2021. If you do not see guidance on a specific topic in the Resources Section in PHAST, please contact the OCHHA ADS Office.

Section References

Carcinogens without CREGs

[U.S. EPA] U.S. Environmental Protection Agency. 1992. EPA's Approach for Assessing the Risks Associated with Chronic Exposure to Carcinogens Background Document 2, January 17, 1992. Available at: http://www.epa.gov/iris/epas-approach-assessing-risks-associated-chronic-exposure-carcinogens

[U.S. EPA] U.S. Environmental Protection Agency. Guidelines for Carcinogenic Risk Assessment. Risk Assessment Forum, U.S. EPA, Wash DC. EPA/630/P-03/001F. Available at: https://www.epa.gov/sites/production/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf

PHAST V1.8 Updates

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[ATSDR] Agency for Toxic Substances and Disease Registry. 2018. Exposure Dose Guidance for Soil and Sediment Ingestion. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, Sept 25.

[ATSDR] Agency for Toxic Substances and Disease Registry. 2016. Exposure Dose Guidance for Water Ingestion. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, Oct 26.

[BLS] Bureau of Labor Statistics. U.S. Department of Labor. 2019. American Time Use Survey, Tables 2 and 4. Available at https://www.bls.gov/news.release/archives/atus_06192019.htm.

[BLS] Bureau of Labor Statistics, U.S. Department of Labor. 2020. Table 3. Available at https://www.bls.gov/news.release/pdf/tenure.pdf.

Copeland, C. Employee Benefit Research Institute. Trends in Employee Tenure, 1983–2018, Figure 1 (February 2019): https://www.ebri.org/docs/default-source/ebri-issue-brief/ebri_ib_474_tenure-28feb19.pdf?sfvrsn=70053f2f_13.

[U.S. EPA] U.S. Environmental Protection Agency. 2011. Exposure Factors Handbook, Chapter 16, "Activity Patterns." Table 16-105.

[U.S. EPA]. U.S. Environmental Protection Agency. 2021. Integrated Risk Information System (IRIS). Vinyl Chloride. Available at: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=1001, January 25.

Updates to the Guidance for Inhalation Exposures

[ATSDR] Agency for Toxic Substances and Disease Registry. 2020. Guidance for Inhalation Exposures. Atlanta, Ga: U.S. Department of Health and Human Services, Public Health Service, December 1.

Lingering VOC (Volatile Organic Compound) Groundwater Plumes and VI (Vapor Intrusion)

[ATSDR] Agency for Toxic Substances and Disease Registry. 2016. Evaluating Vapor Intrusion Pathways – Guidance for ATSDR's Division of Community Health Investigations. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, Oct 31.

[ATSDR] Agency for Toxic Substances and Disease Registry. 2019a. Vapor Intrusion Conceptual Site Model Figure. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, Dec.

[ATSDR] Agency for Toxic Substances and Disease Registry. 2019b. Vapor Intrusion Data Quality Evaluation Worksheet. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, Jan.

Schuver HJ, Steck DJ. Cost-Effective Rapid and Long-Term Screening of Chemical Vapor Intrusion (CVI) Potential: Across Both Space and Time. Remediation. Autumn 2019: 27-53. https://onlinelibrary.wiley.com/doi/abs/10.1002/rem.21439.