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Guidance for Inhalation Exposures

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1. Definitions

Acute exposures: Exposure durations up to 14 days. Exposure concentrations for acute exposure scenarios should be evaluated using acute inhalation minimal risk levels (MRLs) or appropriate toxicity information (e.g., using studies of similar duration if available).

Averaging time (AT): The period over which the exposure is averaged to arrive at a time-weighted exposure factor. For assessing cancer risks, AT is averaged over a lifetime (78 years); for assessing non-cancer hazards, AT is averaged over the exposure duration (days, weeks, or years), which may or may not be a lifetime.

Central tendency exposure (CTE): CTE refers to individuals who have average or typical exposure to a contaminant.

Chronic exposures: Exposure durations greater than 365 days. EPCs derived for chronic exposure scenarios should be evaluated using chronic inhalation MRLs, RfCs, or other suitable health guidance values.

Comparison value (CV): Calculated concentration of a substance in air, water, food, or soil below which it is unlikely to cause harmful (adverse) health effects in exposed people. The CV is used as a screening level during the public health assessment process. Substances found in amounts greater than their CVs should be selected for further evaluation in the public health assessment process.

Exposure duration (ED): The period over which the exposure takes place.

Exposure factor (EF): An expression of how often and how long a person may be contacting a substance in the environment. In many instances, the exposure factor (EF) will equal 1, representing a daily, continuous exposure to the contaminant. However, some exposures may occur on an intermittent or irregular basis; therefore, the EF can be less than one.

Exposure point concentration (EPC): The representative contaminant concentration within an exposure unit or area in an exposure pathway to which people are exposed for acute, intermediate, or chronic durations during the past, present, or future.

Health assessor: A staff scientist with ATSDR or an APPLETREE partner that investigates the public health significance of exposure to hazardous waste. Health assessors usually have bachelor’s, master’s, or doctorate degrees in the biological sciences, geological sciences, environmental engineering, radiation, or public health. Health assessors report their findings in documents, such as public health assessments and public health consultations.

Inhalation rate (IR): The volume of air inhaled over a specified timeframe (e.g. cubic meters per day (m^3/day)).

Intermediate exposures: Exposure durations of 15 to 364 days. EPCs derived for intermediate exposure scenarios should be evaluated using intermediate MRLs or appropriate toxicity information (e.g. using studies of similar duration if available).

Minimal risk level (MRL): An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse non-cancer health effects over a specified duration of exposure. MRLs are calculated for a route of exposure (inhalation or oral) over a specified time period (acute, intermediate, or chronic). MRLs are based on non-cancerous health effects only and do not consider carcinogenic effects. MRLs should not be used as predictors of harmful (adverse) health effects.

Reference concentration (RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups), which is likely to be without an appreciable risk of deleterious non-cancer effects during a lifetime.

Residential occupancy period (ROP): The time in years between when a person moves into a residence and when the person moves out or dies.

Reasonable maximum exposure (RME): RME refers to the high end of the exposure distribution (approximately the 95th percentile) for the exposed population. The RME scenario is intended to assess exposures that are higher than average but are still within a realistic range of exposure.

2. Purpose

This inhalation exposure dose guidance (EDG) provides health assessors with guidance on how to estimate air-related exposures to contaminants of concern based on a variety of exposure scenarios including residential, workplace, and school.

Based on the availability of current exposure parameters, many from the 2011 Exposure Factors Handbook (EFH) published by the U.S. Environmental Protection Agency (U.S. EPA), assumptions used in air assessment public health evaluations must reflect the best available science. This air guidance for inhalation exposure provides health assessors with updated information on how to estimate exposure from inhaling contaminants present in ambient or indoor air.

3. Background

Health assessors evaluate all relevant human exposure pathways, including the inhalation pathway. Inhalation exposures are initially evaluated using health-based comparison values (CVs) and other health guidelines. CVs are media-specific substance air concentrations derived from health guidelines using default exposure assumptions and are used to screen contaminants in air for further evaluation. ATSDR CVs include environmental media evaluation guides (EMEGs), reference dose media evaluation guides (RMEGs), and cancer risk evaluation guides (CREGs). Health guidelines are substance-specific doses or air concentrations derived using toxicologic information. Where adequate dose-response or concentration-response data exist, health guidelines are derived for oral and inhalation exposure. Health guidelines include ATSDR's minimal risk levels (MRLs)[1], EPA reference doses (RfDs), and EPA reference concentrations (RfCs). These health guidelines are for non-cancerous endpoints. When an inhalation MRL or RfC is based on a study with intermittent exposure (e.g., 8 hr/day), the study concentration is usually adjusted to a continuous 24-hour exposure. Thus, health assessors will usually need to adjust the site-specific exposure point concentration (EPC) to a continuous, daily exposure. Exceptions to this rule are described in a text box later in this guidance document. And finally, when evaluating the risk of cancer, ATSDR uses EPA's cancer slope factor and inhalation unit risk approach for estimating site-specific cancer risk.

When possible, health guidelines frequently have dosimetric adjustments to account for differences in chemical properties, developmental and physiological differences in humans, and human health outcomes modeled from animal studies. This guidance, such as benchmark dose modeling, gives information on exposure data considerations, exposure default values and considerations used to characterize a variety of populations, and examples of inhalation exposure evaluations from common exposure scenarios. Doses in mg/kg/day are usually not calculated for the inhalation pathway, except in special cases where inhalation and oral exposures occur simultaneously for a contaminant that targets the same organ or system for both oral and inhalation routes. More information on combining the inhalation and oral pathways is provided in ATSDR's EDG for the SHOWER model (ATSDR 2018b).

4. Steps a health assessor should take prior to those outlined in this guidance

Prior to the steps outlined in this guidance document, the health assessor will have obtained and analyzed their exposure data, identified the presence of a completed exposure pathway, screened the data against health-based comparison values, and identified the contaminants of concern in the dataset.

This guidance should be used after the initial CV screening process, and the contaminants of concern have been identified, but before the health assessor determines the public health implications of contaminant exposures. As part of the public health implications, health assessors

[1] https://www.atsdr.cdc.gov/hac/phamanual/appf.html

should adjust the EPC with the appropriate exposure factors, particularly when intermittent exposures are involved. Health assessors will compare the adjusted EPC to inhalation health guidelines and, if exceeded, to non-cancer toxicity values. For carcinogens, health assessors will use inhalation unit risk values to estimate cancer risk.

EPCs are air contaminant concentrations that serve as the basis for an air assessment along with ratios called exposure factors (EFs), which consider exposure time and frequency. See the ATSDR EPC guidance document for more information on using site-specific EFs to calculate EPCs (ATSDR, 2019).

5. Calculation of exposure factors (EFs)

Several variables are considered in calculating the exposure factor (EF) used to adjust cancer and non-cancer risks. Identifying the exposed individuals and the location of exposure are the two variables that informs the assumptions about the frequency and duration of exposures. These variables and their use in computing the EF are discussed below.

5.1 Identifying the exposed population

Exposed individuals are defined by site-specific exposure scenarios (e.g., workplace, residence, daycare facility). In each scenario, health assessors should determine if certain groups might be more sensitive to airborne pollutants. For pollutant exposure via inhalation, newborns and young toddlers are generally at risk for the highest exposure, because their airways are not yet mature and they have different ventilation rates (Appendix A, Table A-3). Several studies support children being a sensitive population (Dietert et al. 2000; Foos et al. 2008; Ginsberg et al. 2008). The site of toxicity for children and adults is also dependent on chemical properties (e.g., gas versus particulate, irritant, solubility, lipophilicity, etc.). Many of these physiological and chemical factors are important factors in toxicity when deriving MRLs[2], RfDs, and RfCs. In residential scenarios, the very young or very old, and those with compromised health (e.g., cardiovascular or respiratory conditions) are usually considered sensitive populations. More information about sensitive groups is available in ATSDR's toxicological profiles.

5.2 Exposure factor adjustments

Understanding the activity patterns of the population being evaluated informs assumptions about the components used to compute the exposure factor (EF). For example, if evaluating a workplace or an early childcare and education facility (e.g., daycare, schools), the health assessor will need to factor in the population of concern not being exposed for 24 hours a day for 7 days a week. This is done by adjusting the EPC from intermittent exposure (e.g., 8 hr/day, 5 days/week, 50 wks/year) to continuous 24-hour exposure. Examples are provided in Appendix C.

If health assessors are evaluating an elderly population living in a nursing home, they can reasonably assume that patients are exposed 24-hours a day. Thus, the EPC remains the same because the EF equals 1 (e.g., 24/day, 7 days/week, 52 wks/year) Health assessors can use

[2] https://www.atsdr.cdc.gov/mrls/compendium_of_papers_on_mrls_and_health_effects.html

ATSDR default assumptions or site-specific activity data, if warranted. Chapter 16 of U.S. EPA's Exposure Factors Handbook (EFH) is dedicated to activities that define the "where" of exposure (U.S. EPA, 2011). The "where" explains which assumptions are appropriate to calculate exposure factors for activities indoors and outdoors and time spent in various places throughout the day (home, school, daycare, etc.).

5.2.1 Chronic Exposures

ATSDR defines a chronic exposure as exposure to a chemical for a period of 365 days or more.

Residential scenarios

- ATSDR recommends the use of an average life expectancy value of **78 years** for adults (both males and females). For assessments where exposures are gender-specific, life expectancy values of **75 years for men and 80 years for women** are recommended (ATSDR 2016a).
- The 95th percentile (*reasonable maximum exposure* or RME) residential occupancy period (ROP: length of time a person resides in a specific property) is 33 years and the 50th percentile (*central tendency exposure* or CTE) ROP is 12 years (ATSDR 2016a).
- The exposure factor for residential scenarios is generally assumed to be daily (24 hours a day, 365 days a year), resulting in an EF = 1 for *non-cancer* residential health outcomes and an appropriately adjusted EF for *cancer* residential health outcomes (the site-specific exposure duration over a lifetime, in years).

Using the reasonable maximum exposure (RME) conditions (i.e., 95th percentile residential occupancy period of 33 years), the EF for non-cancer chronic residential exposure is (ATSDR 2016a)

$$(1)\quad EF_{noncancer\ chronic} = \frac{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 33\ yr}{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 33\ yr} = 1$$

In the same scenario, the EF for cancer assessment is

$$(2)\quad EF_{cancer,\ chronic} = \frac{24\frac{hr}{d}x\ 7\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 33\ yr}{24\frac{hr}{d}x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 78\ yr} = 0.42$$

The default assumption for residential air evaluations is 24-hour exposure. Health assessors, however, may be asked to evaluate unique circumstances for residential exposures. If the evaluation requires an understanding and calculation of indoor and outdoor exposure to calculate total inhalation exposure for a given time frame, some additional values are given in Appendix B. A site-specific justification must be provided in the public health document if the health assessor is using a different value than the default 24-hour exposure.

Vapors off-gassed during showering from contaminated water can result in elevated indoor multi-route exposures. The multi-route exposures are briefly discussed in Section 5.

Childcare/school exposure scenarios

Health assessors may be requested to assess exposures for children in childcare facilities as well as traditional preschool, elementary, middle, and high school scenarios. The ATSDR default assumptions are presented for daycare facilities in Table 1a and for kindergartens and grade schools in Table 1b. Default parameters for CTE and RME exposures in Tables 1a and 1b are based on the EFH (2011) Chapter 16 and U.S. Department of Education publication (Snyder *et al.* 2018).

As a default assumption, children could be exposed in a daycare or school environment for five out of seven days per week. Health assessors should modify this assumption based on site-specific conditions if children are exposed for less than or more than five days a week.

Table 1a. 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 [a]	11.8 [a]	50	52.14
1 to <2 years	4.8 [a]	9.9 [a]	50	52.14
2 to <6 years[b]	6.4	9.6	50	52.14

Source unless otherwise noted: Exposure Factors Handbook (2011), Chapter 16, "Activity Patterns." Table 16-11.

[a] *The CTE (central tendency estimate) and RME (reasonable maximum exposures) for children under 2 years were obtained from Table 16-18, because table 16-11 did not represent sufficient data (number of children) to generate reliable statistics for these age categories.*

[b] *The daily CTE/RME for 2- to <6-year-olds was calculated by weighting the averages for 2- to <3- and 3- to <6-year-olds in table 16-17 to adhere to the ATSDR standard age category of 2 to <6 years:*

$CTE_{2\ \text{to}\ <6\ \text{years}}$: 4.5 hrs/day*0.25 (2 to <3 years) + 7 hrs/day*0.75 (3 to <6 years)= 1.125+5.23 = 6.4 hrs/day

$RME_{2\ \text{to}\ <6\ \text{years}}$: 8.8 hrs/day*0.25 (2 to <3 years) + 9.83 hrs/day*0.75 (3 to <6 years)= 2.2+7.4 = 9.6 hrs/day

**The CTE assumption accounts for families taking 2 weeks of vacation each year. RME assumes year-round daycare for younger children. Using the custom group feature in PHAST, the user may specify additional exposure duration for special considerations, such as children attending a different duration childcare during the summer months.*

Table 1b. Children: time per day spent in grade school pre-kindergarten through 12¶

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

¶*Source unless otherwise noted: Exposure Factors Handbook (2011), Chapter 16, "Activity Patterns." Table 16-11.*
[a]Snyder, T.D., de Brey, C., and Dillow, S.A. 2018. *Digest of Education Statistics 2018* (NCES 2016-014). National Center for Education Statistics, Institute of Education Sciences, U.S. Dept of Education. Washington, DC. (Table 203.90)
**The CTE assumption accounts for winter, spring, and summer breaks of 13 total weeks away from school, yielding a CTE assumption of 39/52.14 weeks a year of school exposure; the RME assumption is that children attend summer school or school-based camps for 8 weeks of the summer at the same location, yielding an RME assumption of 47/52.14 weeks a year of school exposure. Using the custom group feature in PHAST, the user may specify additional exposure duration for special considerations, such as children attending a different duration summer school during the summer months.*

Additional information for parameters in Tables 1a and 1b

- The childcare and preschool annual CTE assumes exposures for children of workers with time away from daycare (e.g., vacation, sickness), whereas the annual RME assumes no vacation for these workers. The health assessor may choose to change this assumption if they have site-specific data that indicates that children attend the childcare facility for other durations.
- ATSDR recommends the CTE assumption account for winter, spring, and summer breaks of 13 total weeks away from school, yielding a CTE assumption of 39/52.14 weeks a year of school exposure; the RME assumption is that children attend summer school or school-based camps for 8 weeks of the summer, yielding an RME assumption of 47/52.14 weeks a year of school exposure. The user may specify additional exposure duration for special considerations, such as children attending a different duration of summer school or childcare during the summer months.
- If an assessment of a child in various exposure scenarios is required, EFH (EPA, 2011) has detailed information about the number of hours children spend indoors/outdoors at home, indoors at childcare/school, and outdoors at childcare/school. Table B-1, Appendix B provides information from the EFH, Chapter 16 (EPA, 2011), on typical time spent indoors/outdoors in childcare/preschool/school and at home for children through age 18. Additional information is also provided in Table B-2 for how much time adults spend at home compared to outdoors.
- For elementary school children chronically exposed to a carcinogen at school from kindergarten through fifth grade (i.e., the 6 to <11 years age group), we can calculate the EF for the school term assuming multi-year, chronic exposure. In this instance, the school term is 9 months, and the average (CTE) exposure duration is 6.7 hours a day, 5 days a week for 39 weeks over five years. The non-cancer risk for this pollutant can be calculated with the following equation:

$$(3)\quad EF_{noncancer,\ chronic} = \frac{6.7\,\frac{hr}{d}\ x\ 5\,\frac{d}{wk}\ x\ 39\ wk\ x\ 5\ yr}{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\ wk\ x\ 5\ yr} = 0.15$$

While the EF for cancer risk can be calculated using this equation:

$$(4)\quad EF_{cancer,\ chronic} = \frac{6.7\,\frac{hr}{d}\ x\ 5\,\frac{d}{wk}\ x\ 39\ wk\ x\ 5\ yr}{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\ wk\ x\ 78\ yr} = 0.0095$$

Commercial/industrial scenarios

- ATSDR recommends that health assessors assume a full-time worker exposure scenario of 8.5 hours a day (8.5 hr/24 hr), 5 days a week (5 days/7 days) for 50 weeks per year for 20 years (RME) and 8.5 hours a day (8.5 hr/24 hr), 5 days a week (5 days/7 days) for 50 weeks per year for 5 years (CTE), unless site-specific conditions warrant an adjustment to these standard assumptions. For part-time employees, health assessors should use 5.1 hrs/day (5.1 hr/24 hr), 5 days a week (5 days/7 days) for 50 weeks per year for 3.1 years (CTE) unless site-specific conditions warrant an adjustment. Table 2 summarizes these assumptions for site-specific assessments.

Table 2. Default assumptions for occupational exposure scenarios

Typical workday, all (hrs/day)[a]	Work year (weeks)	Work tenure (years)
Full time: 8.5 hrs	RME: 50.0 CTE: 50.0	RME: 20.0 years[b] CTE: 5.0 years[c]
Part time: 5.1 hrs	CTE: 50.0	CTE: 3.1 years[d]

[a] *Bureau of Labor Statistics, U.S. Department of Labor, American Time Use Survey, weekday work hours, Table 2, Table 4 (June 2019): https://www.bls.gov/news.release/archives/atus_06192019.htm*
[b] The RME work tenure reflects the tenure of 20 years or more for the top 10% of the longest employed workers. *Bureau of Labor Statistics, U.S. Department of Labor, Employee Tenure in 2020, Table 3 (September 2020):* https://www.bls.gov/news.release/pdf/tenure.pdf. Distribution of employed wage and salary workers by tenure with current employer, age, sex, race, and Hispanic and Latino ethnicity, January 2020."
[c] *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*
[d] *Exposure Factors Handbook (2011), Chapter 16, "Activity Patterns." Table 16-105.*

- Health assessors should assume an individual works 20 years at the same location unless site-specific conditions warrant another exposure duration. Note that 20 years represents the 90th percentile estimate of tenure (RME) with current employer from the Bureau of Labor Statistics as of September 2018. In 2018, workers 25 years and older had a *median* tenure (CTE) of 5 years. ATSDR selected these values for CTE and RME occupational tenures.

Using RME exposure conditions (i.e., 90th percentile work tenure of 20 years and a 50 wks/yr, 5 d/wk, 8.5 hr/day exposure), the EF for non-cancer chronic occupational exposure is (ATSDR 2016a)

$$(5)\quad EF_{noncancer\ chronic} = \frac{8.5\,\frac{hr}{d}\ x\ 5\,\frac{d}{wk}\ x\ 50\,\frac{wk}{yr}\ x\ 20\ yr}{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 20\ yr} = 0.24$$

In the same occupational exposure scenario, the EF for cancer assessment is

$$(6)\quad EF_{cancer,\ chronic} = \frac{8.5\,\frac{hr}{d}\ x\ 5\,\frac{d}{wk}\ x\ 50\,\frac{wk}{yr}\ x\ 20\ yr}{24\frac{hr}{d}x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 78\ yr} = 0.06$$

5.2.2 Intermediate Exposures

ATSDR defines intermediate exposure as exposure to a chemical for a period of 15 to 364 days. Exposures that occur for 3 weeks or for 36 weeks (i.e., 9 months) are both classified as intermediate exposures. For exposures of intermediate duration, the exposure is adjusted to the duration of the scenario using exposure factors.

For example, for elementary school children exposed at school for a single school year, we can calculate the EF for the school term assuming intermittent exposure. In this instance, the school term is 39 weeks (a little over 9 months), and the average (CTE) exposure duration is 6.7 hours a day, 5 days a week for 39 weeks:

$$(7)\quad EF_{intermediate} = \frac{6.7\,\frac{hr}{d}\ x\ 5\,\frac{d}{wk}\ x\ 39\ wk}{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 39\ wk} = 0.20$$

5.2.3 Acute Exposures

ATSDR defines acute exposure as exposure to a pollutant for a duration of 14 days or less. Acute exposures that occur for this time period should be adjusted for the exposure duration of the scenario. For example, if children are exposed to a pollutant at an elementary school via inhalation for 6.7 hours a day for 5 days, this acute exposure should be adjusted as follows (see inset for exceptions to this adjustment):

$$(8)\quad EF_{acute} = \frac{6.7\,\frac{hr}{d}\ x\ 5\frac{d}{wk}}{24\,\frac{hr}{d}\ x\ 5\,\frac{d}{wk}} = 0.28$$

Exceptions for exposure factor adjustment

As mentioned previously, when site exposure is intermittent (e.g., 8 hr/day), the EPC is usually adjusted to a 24-hour continuous exposure by including 8/24 as part of the EF term.

Exceptions to this rule for adjusting the noncancer acute inhalation exposure to a 24-hr continuous exposure include these chemicals: ammonia, hydrogen sulfide, chloroform, sulfur dioxide, formaldehyde, 2-butanone, and acetone. If the target population has acute, inhalation exposure to these chemicals, the concentration should not be adjusted to a continuous 24-hr concentration. The reason the site-specific EPC is not adjusted for these pollutants is because the acute inhalation MRL was derived using the unadjusted study concentration. That is, the toxicity value used to derive the MRL was not adjusted to a continuous 24 hr exposure (ATSDR 2016a).

The same is true for intermediate and chronic exposure for chloroform and formaldehyde. The site-specific EPC should not be adjusted from intermittent to continuous because the intermediate and chronic MRLs for these two chemicals used the unadjusted study concentration to derive the MRL. The noncancer EF for these two chemicals should be 1. However, when calculating cancer risk, the chronic cancer EF for these two chemicals should be adjusted.

See the EDG for Determining Life Expectancy and Exposure Factor for more details (ATSDR 2016a).

The exposure factor discussed above assumes the school children have only been exposed for a single week; in many cases school exposure represents a chronic period, and as such would be assessed using the RME chronic EF above.

Note that ATSDR's MRL guidance states that acute exposure factors should be adjusted to a 24-hr (daily) continuous exposure and not to a weekly exposure. For exceptions to this guidance, see text box: exceptions for exposure factor adjustment.

6. Assessing exposure

For most sites, ATSDR relies on health guidelines to evaluate non-cancer endpoints when a selected contaminant needs further toxicological evaluation. Health guidelines are based on a "critical study," which represents the most well-documented study available for the most sensitive health endpoint (organ or body system) identified. Critical studies can be animal studies, but also can be human population-based studies. The critical study is used to derive the health guidelines (e.g., inhalation MRL, RfC). These are estimates of the daily human exposure concentration to a hazardous substance over a specified duration that are likely to be without appreciable risk of adverse non-cancer health effects. Carcinogenic effects are not considered in deriving an MRL or RfC.

Please note that to combine the risk of exposure to multiple pollutants, the chemicals must affect the same target organ, based on citations in the ATSDR Toxicological Profiles or the EPA IRIS file. Further, health assessors should use the appropriate time integrated EPC (e.g., 24-hour, annual average, etc.) for the equivalent risk duration (acute, chronic, respectively). When these conditions are met, health assessors can combine non-cancer risk to calculate a combined non-cancer hazard index. Please refer to the ATSDR *Framework for Assessing Health Impacts of Multiple Chemicals and Other Stressors (Update) (2018)*[3] for specific methods of conducting a multi-pollutant risk evaluation.

6.1 The standard approach for non-cancer assessments

The likelihood of non-cancer health hazards can be evaluated by calculating hazard quotients (HQ) for individual contaminants. A hazard quotient is the ratio of the EPC to a non-cancer health guideline, such as an inhalation MRL or RfC.

$$(9)\quad HQ\ (unitless) = \frac{EPC\ (\frac{ug}{m3}) * EF}{Inhalation\ MRL\ (\frac{ug}{m3})}$$

The inhalation MRL is the concentration of a pollutant in air that is unlikely to cause non-cancerous harmful effects for the specified duration of exposure. ATSDR has inhalation MRLs for acute (less than 14 days), intermediate (15 days to 364 days), and chronic (1 year or more) exposures (ATSDR 2005a). The MRL selected should be appropriate for the exposure duration. U.S. EPA's RfCs are developed for chronic exposure. If the HQ calculated is equal to or less than 1, non-cancer adverse health effects are not expected to result from exposure to the

[3] https://www.atsdr.cdc.gov/interactionprofiles/ip-ga/ipga.pdf

pollutant. If the HQ is greater than 1, further toxicological evaluation is warranted by reviewing the critical and supporting studies used to develop the health guideline.

6.2 The standard approach for cancer assessments[4]

Cancer risk can be calculated using the adjusted EPC and the U.S. EPA inhalation unit risk (IUR) for cancer. The U.S. EPA IUR is the incremental risk posed by a specific concentration unit in air (usually per 1 microgram per cubic meter ($\mu g/m^3$) of the pollutant in air). The calculation yields the relative increase of cancer risk (above the background rate) from exposure to individual pollutants (ATSDR 2005a).

Cancer risk can be calculated by multiplying the long-term air concentration by the IUR, adjusting the duration of exposure using the appropriate exposure factor calculation[5]:

$$(10)\quad \textit{Cancer risk} = IUR \times EPC\ (\mu g/m^3) \times EF$$

6.3 Dose calculation for multi-route exposures during showering

ATSDR's approach for evaluating inhalation exposure is to use air concentrations. Thus, the air concentrations calculated for an exposed population are compared to the air concentrations from human or animal studies to decide the harmful effects that might be possible. However, when persons are exposed not only by inhalation but also by other pathways, typically drinking water, it is sometimes appropriate to combine the exposure from both pathways. To combine the exposure from inhaling a chemical with the exposure from drinking contaminated water, the inhalation exposure has to be converted to a dose in mg/kg/day.

The most common of these multiple route scenarios is when household water is contaminated, and residents are not only showering or bathing in the water but are also drinking the water. In this special case, ATSDR uses its SHOWER model to estimate inhalation exposure, which is then converted to a dose. The SHOWER model also estimates the dermal dose from skin contact while bathing and washing hands. ATSDR's public health assessment site tool (PHAST) is used to estimate the drinking water dose. All three doses can be combined to generate a total dose that can be used to determine possible health effects. ATSDR applies certain limitations, though, when combining exposure from multiple routes. The chemical must target the same organs or system for both the inhalation and the oral pathways. More information about this approach, including a list of approved chemicals, can be found in ATSDR's EDG for the SHOWER Model (ATSDR, 2018a).

6.4 Special considerations

Aside from the special considerations mentioned in this section, health assessors should consult with air SMEs to discuss scenarios or specific pollutants (e.g., particulates vs aerosols) that are not identified in this guidance.

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[4] See section 5.4 "Special Considerations" for a discussion on evaluating mutagenic pollutants.
[5] https://www.epa.gov/sites/production/files/2015-09/documents/partf_200901_final.pdf, p.22.

6.4.1 Mutagens

Mutagens are agents that can cause changes in the DNA of the exposed individual. These changes can cause cancer or other serious health effects. Pollutants that cause cancer from a mutagenic mode of action may result in a higher risk of cancer for children exposed in early life than for adults. Mutagens are identified in the U.S. EPA Regional Screening Level (RSL) table (https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables) and require an additional step for risk assessment purposes.

U.S. EPA has proposed that risk calculations for chemicals that act with a mutagenic mode of action (MOA) for carcinogenesis can be quantified using age-dependent adjustment factors (ADAFs), and in the unique case of vinyl choride, age-specific cancer slope factors (CSFs) (U.S. EPA 2009). For the standard ATSDR age ranges, ADAF adjustments are shown in Table 3.

Table 3. ATSDR age dependent adjustment factors

Age Range	ADAF
Birth to <1 year	10
1 to <2 years	10
2 to <6 years	3
6 to <11 years	3
11 to <16 years	3
16 to <21 years	1
>21 years	1

This adjustment for lifetime risk using the inhalation unit risk value for mutagenic pollutants is

$$(11)\quad Risk = (IUR \times EPC_{birth\ to\ <1\ yr} \times EF \times ADAF_{birth\ to\ <1\ yr}) + (IUR \times EPC_{1\ to\ <2\ yrs} \times EF \times ADAF_{1\ to\ <2\ yrs}) + (IUR \times EPC_{2\ to\ <6\ yrs} \times EF \times ADAF_{2yr\ to\ <6\ yrs}) + (IUR \times EPC_{6\ to\ <11\ yrs} \times EF \times ADAF_{6\ to\ <11\ yrs}) + (IUR \times EPC_{11\ to\ <16\ yrs} \times EF \times ADAF_{11\ to\ <16\ yrs}) + (IUR \times EPC_{16\ to\ >21yrs} \times EF) + (IUR \times EPC_{>21yrs} \times EF)$$

Examples: Mutagenic MOA adjustments with the same and with different exposures
Residential air samples over the summer are available for a home, where an EPC of 0.0005 $\mu g/m^3$ has been established. Children in this household are assumed to be exposed from birth until 21 years of age. Adults are assumed to be exposed for 33 years (the 95th percentile residential occupancy period). Note that the carcinogen has a mutagenic MOA, for which the inhalation unit risk is 0.084 $(\mu g/m^3)^{-1}$.

To calculate the cancer risk for a population with an average life expectancy of 78 years, sum the risk associated with each of ATSDR's standard age ranges (Note: adult residential occupancy is assumed to be 33 years; see section 4.2).

- Scenario 1 (Table 4) describes cancer risk for constant exposure over a lifetime to an upwind community with lower average concentrations of the pollutant, while Scenario 2 (table 5) describes cancer risk where one age range is disproportionately exposed to the pollutant being evaluated.

- In Scenario 2, assume we are evaluating exposures at a nearby downwind preschool where children aged 2 to 5 years are exposed to emissions from the facility as well as in their upwind residence. Note that lifetime risk is calculated by summing the child and adult exposure for the appropriate number of years.

Table 4. Scenario 1: The same exposure concentration is expected for children and adults

<table>
<tr><th>Exposure group</th><th>IUR ($\mu g/m^3)^{-1}$</th><th>EPC ($\mu g/m^3)^*$</th><th>ADAF (unitless)</th><th>Exposure duration/lifetime exposure (yr/yr)¶</th><th>Risk</th></tr>
<tr><td>Birth to <1 yr</td><td rowspan="8">0.084</td><td rowspan="8">0.0005</td><td>10</td><td>1/78</td><td>5.4×10^{-6}</td></tr>
<tr><td>1 to <2 yrs</td><td>10</td><td>1/78</td><td>5.4×10^{-6}</td></tr>
<tr><td>2 to <6 yrs</td><td>3</td><td>4/78</td><td>6.5×10^{-6}</td></tr>
<tr><td>6 to <11 yrs</td><td>3</td><td>5/78</td><td>8.1×10^{-6}</td></tr>
<tr><td>11 to <16 yrs</td><td>3</td><td>5/78</td><td>8.1×10^{-6}</td></tr>
<tr><td>16 to <21 yrs</td><td>1</td><td>5/78</td><td>2.7×10^{-6}</td></tr>
<tr><td>Total Childhood Exposure</td><td></td><td>21 years</td><td>3.6×10^{-5}</td></tr>
<tr><td>Adults ≥21 yrs</td><td>1</td><td>33/78</td><td>1.8×10^{-5}</td></tr>
</table>

**This approach assumes that the EPC is the same throughout exposure.*
¶Assumes a residential scenario where children are exposed for 21 years and adults are exposed for 33 years (the 95th percentile residential occupancy period)

Table 5. Scenario 2. Different exposure concentration is expected for children aged 2 to <6 years

<table>
<tr><th>Exposure group</th><th>IUR ($\mu g/m^3)^{-1}$</th><th>EPC ($\mu g/m^3$)</th><th>ADAF (unitless)</th><th>Exposure duration/lifetime exposure (yr/yr)¶</th><th>Risk</th></tr>
<tr><td>Birth to <1 yr</td><td rowspan="8">0.084</td><td rowspan="2">0.0005</td><td>10</td><td>1/78</td><td>5.4×10^{-6}</td></tr>
<tr><td>1 to <2 yrs</td><td>10</td><td>1/78</td><td>5.4×10^{-6}</td></tr>
<tr><td>2 to <6 yrs</td><td>0.01</td><td>3</td><td>4/78</td><td>1.3×10^{-4}</td></tr>
<tr><td>6 to <11 yrs</td><td rowspan="5">0.0005</td><td>3</td><td>5/78</td><td>8.1×10^{-6}</td></tr>
<tr><td>11 to <16 yrs</td><td>3</td><td>5/78</td><td>8.1×10^{-6}</td></tr>
<tr><td>16 to <21 yrs</td><td>1</td><td>5/78</td><td>2.7×10^{-6}</td></tr>
<tr><td>Total Childhood Exposure</td><td></td><td>21 years</td><td>1.6×10^{-4}</td></tr>
<tr><td>21 to 78 yrs
Adulthood Exposure</td><td>1</td><td>33/78</td><td>1.8×10^{-5}</td></tr>
</table>

¶Assumes a residential scenario where children are exposed for 21 years and adults are exposed for 33 years (the 95th percentile residential occupancy period)

6.4.2 Increased ventilation rates

Daily air intake rates (m^3/day) for children and adults account for variation in breathing (ventilation) rates (m^3/min or m^3/hr) during typical activities during the day. Therefore, ventilation rates are not generally used to evaluate exposure unless inhalation exposure occurs during a specific during specific activities (e.g. intense physical exertion, showering). In situations such as exercise facilities, where ventilation rates are higher than normal, it is appropriate to adjust the EF using a scaling factor of the increased breathing rate over the normal default value. Table 6 shows suggested increased breathing rates for moderate and intense activities for ATSDR's standard age groups, based on information from the Exposure Factors Handbook (EPA 2011).

Thus, the EF becomes

$$(12)\quad EF = \left(\frac{Elevated\ Breathing\ Rate\ (\frac{m3}{day})}{Default\ Breathing\ Rate\ (\frac{m3}{day})} \right) \text{x}\ \frac{F\ x\ ED}{AT}$$

The EF, adjusted by breathing rate, is then used in the previously defined cancer and non-cancer equations (see sections 5.1 and 5.2).

Note that the ATSDR breathing rate values for common scenarios are shown in Table 6. Health assessors should use the long-term default inhalation rate for daily inhalation assumptions. For physical activity, including physical education, recess, and sports, health assessors should use the heavy intensity breathing rate.

TABLE 6. Inhalation rate ratios for use in increased ventilation rate scenarios[a]

Exposure Group	Long term default inhalation rate[b] m^3/min or (m^3/day)[c]	Heavy intensity mean[b] inhalation rate (m^3/min)	Ratio of heavy intensity/default inhalation rate
Birth to <1 year	0.0038 (5.4)	0.0260	6.8
1 to <2 years	0.0056 (8.0)	0.0380	6.8
2 to <6 years	0.0068 (9.8)	0.0375	5.5
6 to <11 years	0.0083 (12.0)	0.0420	5.1
11 to <16 years	0.0106 (15.2)	0.0490	4.6
16 to <21 years	0.0113 (16.3)	0.0490	4.3
>21 years[d]	0.0106 (15.3)	0.0502	4.7
Pregnant Women	0.0147 (21.1)	NC	NC
Nursing Women	0.0158 (22.8)	NC	NC

[a]Mean inhalation rates shown, are combined for males and females and are extracted from Exposure Factors Handbook (2011), Chapter 6, Tables 6-1 (long term) and 6-2 (short term).
[b]The mean values were used because U.S. EPA (2011) noted "… *there may be a high degree of uncertainty associated with the upper percentiles. These values represent unusually high estimates of caloric intake per day and are not representative of the average adult or child*."
[c]Recommended long term inhalation rates, Exposure Factors Handbook (2011), Table 6-1, Chapter 6
[d]Weighted average of adult U.S.EPA age ranges in Table 6-1
NC=not calculated

See Appendix D, Scenario 3 for an example of these adjustments in a scenario of student athletes exposed to benzene emissions at school and during practice. Note that in some instances, adjusting ventilation rates may also be appropriate when evaluating occupational exposures for heavy intensity occupations (e.g., construction).

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APPENDIX A. Inhalation rate tables for risk calculations

This section gives default values for populations for which health assessors may be calculating doses and provides justification for our assumptions on children's sensitivity and vulnerability identified in inhalation dosimetry methodology. Please note that dose calculations are not standard and are only conducted in very limited site-specific scenarios (see Section 5).

Summary of air inhalation rates and body weights

Default inhalation rates are based on the U.S. EPA 2011 Exposure Factors Handbook (EFH) (U.S. EPA 2011). The EFH information about adult and child inhalation rates and body weight is based on recent data from the National Health and Nutrition Examination Survey (NHANES) IV (CDC 2012). Table A-1 describes rates and body weight for default ATSDR age groups. See Tables A-2 and A-3 for expanded detail by smaller age groups. See Table A-4 for more detail on pregnant and lactating women.

Table A-1. Age and activity-specific inhalation rates[a]

Age group	Long term default inhalation rate[b]		Short term mean[b] default inhalation rate by *activity level* (m^3/minute)				
	m^3/day[c]	(m^3/min)[c]	Sleep or nap	Sedentary/ passive	Light intensity	Heavy intensity	Body weight (kg)
Birth to <1 year	5.4	0.0038	0.0030	0.0031	0.0076	0.0260	7.8
1 to <2 years	8.0	0.0056	0.0045	0.0047	0.0120	0.0380	11.4
2 to <6 years	9.8	0.0068	0.0044	0.0046	0.0113	0.0375	17.4
6 to <11 years	12.0	0.0083	0.0045	0.0048	0.0110	0.0420	31.8
11 to <16 years	15.2	0.0106	0.0050	0.0054	0.0130	0.0490	56.8
16 to <21 years	16.3	0.0113	0.0049	0.0053	0.0120	0.0490	71.6
>21 years[d]	15.3	0.0106	0.0050	0.0047	0.0124	0.0502	80.0
Pregnant Women[e]	21.1	0.0147	NA	NA	NA	NA	73.0[f]
Nursing Women[e]	22.8	0.0158	NA	NA	NA	NA	73.0[f]

[a]Mean inhalation rates, shown are combined for males and females, and are extracted from Exposure Factors Handbook (2011), Table 6-1, Chapter 6.
[b]The mean values were used because U.S. EPA (2011) noted "… *there may be a high degree of uncertainty associated with the upper percentiles. These values represent unusually high estimates of caloric intake per day and are not representative of the average adult or child*."
[c]Recommended long term inhalation rates, Exposure Factors Handbook (2011), Table 6-1, Chapter 6.
[d]Weighted average of adult U.S.EPA age ranges in Table 6-1
[e] *Adjusted average (12 years for 11 to <23 yrs [0.267*rate]; 7 years for 23 to <30 yrs [0.156*rate]; 26 years for 30 to 55 yrs [0.578*rate])*
[f]*The ATSDR Body Weight EDG recommends the use of 73 kg as the default body weight for both pregnant/lactating women, based on the 50th percentile weights for all three trimesters of pregnancy as reported in NHANES 1999-2006 data, and the weighted average of women 16-45 years of age (child bearing age) plus 5 kg retained during lactation (ATSDR, 2016b).*
NA=not available

Table A-2. Expanded age and activity-specific inhalation rates[a]

Exposure group	Long term default inhalation rate (m^3/day)[b]	Short term default inhalation rate by *activity level* (m^3/minute)				Body weight (kg)[b]
		Resting mean	Sedentary/ passive mean	Light intensity mean	Heavy intensity mean	
Birth to <1 year[c]	5.4	0.0030	0.0031	0.0076	0.0260	7.8
1 to <2 years	8.0	0.0045	0.0047	0.0120	0.0380	11.4
2 to <3 years	8.9	0.0046	0.0048	0.0120	0.0390	13.8
3 to <6 years	10.1	0.0043	0.0045	0.0110	0.0370	18.6
6 to <11 years	12.0	0.0045	0.0048	0.0110	0.0420	31.8
11 to <16 years	15.2	0.0050	0.0054	0.0130	0.0490	56.8
16 to <21 years	16.3	0.0049	0.0053	0.0120	0.0490	71.6
21 to <31 years	15.7	0.0043	0.0042	0.0120	0.0500	80.0
31 to <41 years	16.0	0.0046	0.0043	0.0120	0.0490	80.0
41 to <51 years	16.0	0.0050	0.0048	0.0130	0.0520	80.0
51 to <61 years	15.7	0.0052	0.0050	0.0130	0.0530	80.0
61 to <71 years	14.2	0.0052	0.0049	0.0120	0.0470	80.0
71 to <81 years	12.9	0.0053	0.0050	0.0120	0.0470	80.0
≥81 years	12.2	0.0052	0.0049	0.0120	0.0480	80.0
Pregnant Women[d]	21.1					73.0
Lactating Women[d]	22.8					73.0

[a]Mean inhalation rates shown, are combined for males and females, and are extracted from (U.S. EPA 2011).
[b]See Table A-3, below, for mean inhalation rates and birth weights for infants younger than 1 year of age.
[c]The age interval of birth to < 1 yr was used to evaluate infants for the inhalation pathway.
[d]The ATSDR Body Weight EDG recommends the use of 73 kg as the default body weight for both pregnant/lactating women, based on the 50th percentile weights for all three trimesters of pregnancy as reported in NHANES 1999-2006 data, and the weighted average of women 16-45 years of age (child bearing age) plus 5 kg retained during lactation (ATSDR, 2016b).

Table A-3. ATSDR recommended inhalation rates and body weights for infants under 1 year

Exposure group	Long term default inhalation rate (m^3/day)	Body weight (kg)
Birth to <1 month	3.6	4.8
1 to <3 months	3.5	5.9
3 to <6 months	4.1	7.4
6 to <12 months	5.4	9.2

Source: Exposure Factors Handbook (2011)

Table A-4. ATSDR recommended inhalation rates for pregnant/lactating women[a]

Inhalation rates (m^3/day) by age and gestation/postnatal dates							
Pregnancy					**Postpartum/lactating**		
Underweight females (*Women with a body mass index of* ***<19.8 kg/m²*** *in pre-pregnancy (EFH, 2011)*)							
Exposure group	**9th wk**	**22nd wk**	**36th wk**	**50th percentile average**	**6th wk**	**27th wk**	**50th percentile average**
11 to <23 yrs	17.34	17.46	17.88	17.56	20.31	20.14	20.23
23 to <30 yrs	19.75	19.8	20.29	19.95	22.23	22.04	22.14
30 to 55 yrs	18.05	18.07	18.73	18.28	20.92	20.74	20.83
Normal weight females (*Women with a body mass index of* ***19.8 to 26.0 kg/m²*** *in pre-pregnancy (EFH, 2011)*)							
Exposure group	**9th wk**	**22nd wk**	**36th wk**	**50th percentile average**	**6th wk**	**27th wk**	**50th percentile average**
11 to <23 yrs	20.26	22.27	23.1	21.88	23.56	23.36	23.46
23 to <30 yrs	18.76	20.89	21.69	20.45	22.11	21.91	22.01
30 to 55 yrs	18.63	20.85	21.73	20.40	22.09	21.9	22.00
Overweight females (*Women with a body mass index of* ***>26.0 kg/m²*** *in pre-pregnancy (EFH, 2011)*)							
Exposure group	**9th wk**	**22nd wk**	**36th wk**	**50th percentile average**	**6th wk**	**27th wk**	**50th percentile average**
11 to <23 yrs	25.38	25.65	25.23	25.42	26.61	26.38	26.50
23 to <30 yrs	23.22	23.51	23.05	23.26	24.45	24.23	24.34
30 to 55 yrs	23.77	23.92	23.4	23.70	24.91	24.69	24.80
Avg IR-all pregnant women				**21.10[b]**	**Avg IR-Lactating Women**		**22.84[b]**

Source: EPA Exposure Factors Handbook (2011), Chapter 6, "Inhalation Rates"
[a]*Values represent the 50th percentile of each age group and gestational/postnatal week*
[b]*Adjusted average (12 years for 11 to <23 yrs [0.267*rate]; 7 years for 23 to <30 yrs [0.156*rate]; 26 years for 30 to 55 yrs [0.578*rate])*

If children are part of a special scenario and are suspected to be exposed, ATSDR recommends evaluating non-cancer levels using the default inhalation rates for a toddler aged 1 to <2 years for initial screening purposes. If these children are at risk from chronic exposure, health assessors should evaluate infants (subgroups shown in Table A-3) for intermediate and acute exposures. Children of these ages have the largest ratio of breathing rate to body weight, thus the highest potential exposure of any age group.

If needed, see the Exposure Factors Handbook (2011) for additional assumptions beyond those provided in this guidance. Otherwise, use the values provided in this guidance when calculating risk or exposure doses. If modifications are made from this guidance, explain the basis of those modifications in the document. The current version of EFH is available at https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252.

APPENDIX B. Tables for time spent indoors/outdoors for children and adults

TABLE B-1. Default daily assumptions for children's time spent at home, school, childcare*

Exposure group	CTE time spent indoors, residential (hr/day)	RME time spent indoors, residential (hr/day)	Time spent indoors, school or childcare (hr/day)	Time spent outdoors, school or playground (hr/day)
< 1 month	24.0	24.0	N/A	Not reported
0 to <1 year	18.5	24.0	5.3	Not reported
1 to <2 years	17.8	24.0	4.8	0.60
2 to <6 years[a]	16.0	22.3	5.3	1.43[d]
6 to <11 years	14.9	21.2	6.6	1.47
11 to <16 years[b]	14.8	21.9	6.7	1.34[e]
16 to <19 years[c]	13.9	21.5	6.7	1.31[c]

**This table was converted to hours from original tables in min/day in the EFH (Ch 16., Table 16-18); note that RME would be equivalent to continuous, 24 hr/day exposure*

[a] CTE average: EFH (2011) notes 1-4 year olds spend an average of 288.5 min/day and that 5-11-year-olds spend an average of 396.3 min/day ***indoors*** at childcare/school; thus, the 2 to <6-year-old range is 288.5*0.75 (2 through 4-year-olds) + 396.3 * 0.25 (5-year-olds) = 216.38 + 99.08 = 315.5 min/day (5.3 hrs/day).

RME average: Table 16-1 presents the 95th percentile min/day spent indoors at the child's residence; to merge the 2 to <3 and 3 to <6 age ranges to conform to ATSDR's age ranges (2 to <6), the weighted average of the two age ranges were calculated as follows: 2 to <3 years (1296 min/day *0.25 [1/4 years in the range]) + (1355 min/day*0.75 [3/4 years in the range]) = 324 + 1016.25 = 1340.25 min/day or 22.3 hrs/day.

[b]Averaged; EFH (2011) notes 5-11-year-olds spend an average of 396.3 min/day and that 12-17-year-olds spend an average of 402.6 min/day ***indoors*** at childcare/school; thus, the 11 to <16-year-old range is 396.3*0.20 (11 year olds) + 402.6 * 0.80 (12-15-year-olds) = 79.3 + 322.1 = 401.4 min/day (6.7 hrs/day).

[c]EFH (2011) only estimates hours in school through age 17; we assume the 12-17-year age range for older school children.

[d]Averaged; EFH (2011) notes 1-4-year-olds spend an average of 85 min/day and 5-11-year-olds spend an average of 88 min/day ***outdoors*** at childcare/school; thus, the 3 to <6-year-old range is 85*0.666 (3 and 4 year olds) + 88 * 0.333 (5 year olds) = 56.6 + 29.3 = 85.9 (86) min/day.

[e]Averaged; EFH (2011) notes 5-11-year-olds spend an average of 88 min/day and that 12-17-year-olds spend an average of 78.7 min/day ***outdoors*** at childcare/school; thus, the 11 to <16-year-old range is 88*0.20 (11 year olds) + 78.7 * 0.80 (12-15-year-olds) = 17.6 + 62.96 = 80.6 min/day (1.4 hr/day).

Table B-2. Default daily assumptions for adults: mean time spent at home and outdoors

Exposure group	CTE time spent indoors at residence (hrs/day)	RME time spent indoors at residence (hrs/day)	Time spent outdoors (hrs/day)
18 to <64 years	15.80	23.8	2.27
65+ Years	19.58	24.0	2.35

Source: Exposure Factors Handbook (2011), Chapter 16, "Activity Patterns."

APPENDIX C. Examples

SCENARIO 1- *Elevated non-cancer risk*: The state environmental enforcement agency has collected heavy metals data in ambient air near a 75-year old smelter for 1 year. The annual average manganese (Mn) concentration is 1.8 µg/m^3 at the monitor 0.15 miles downwind of the smelter. The community near the facility is residential, and both a school and nursing home are located nearby. The state wants public health guidance about whether or not long-term exposure to Mn in the community poses a health threat and whether action should be taken to reduce offsite emissions of heavy metals.

To address this scenario, the health assessor takes the following steps:

Step 1: *Identifying the exposed population*

We know that the community near the site contains children and the elderly, and that people possibly spend 24 hours of their day being exposed to manganese. Since the assessment is designed to evaluate the highest exposed individual, we will assume our young child is home during the day and has near-constant residential exposure.

Step 2: *Identifying exposure point concentrations (EPCs)*

We have 1 sample collected every 6 days for 1 year. The one-year ambient Mn concentration was 1.8 µg/m^3 over this period. Using ATSDR EPC guidance, we identify the EPC of 3.2 µg/m^3 as our 95th upper confidence limit (UCL) of the mean.

Step 3: *Exposure factor adjustments*

According to ATSDR guidance, the health assessor should assume the child evaluated is exposed 24 hours a day, 7 days a week, 52.14 weeks a year. We do not know how much manganese is present indoors but will assume it is equivalent to what they would breathe outdoors. Because this is a continuous residential exposure scenario, no concentration adjustment is needed. Since the smelter has been in business 75 years smelting manganese products, we can assume the releases are long-term (health assessors should always evaluate the likelihood that exposures have changed or stayed the same by evaluating available facility information). The exposure factor calculation for our 1-year dataset is as follows:

$$EF_{chronic} = \frac{24\,\frac{hr}{d}\,x\,7\,\frac{d}{wk}\,x\;52.14\,\frac{wk}{yr}\,x\,1\,yr}{24\,\frac{hr}{d}\,x\,7\,\frac{d}{wk}\,x\,52.14\,\frac{wk}{yr}\,x\,1\,yr} = 1$$

Step 4: *Assessing exposure for the most sensitive person in the population at risk*

Using the site-specific EF for this residential population (EF = 1, our default), we can compare the exposure point concentrations multiplied by the RME exposure factor of 1 to the ATSDR chronic inhalation MRL for manganese of 0.30 µg/m^3 to calculate an RME hazard quotient for long term residents using the following equation (ATSDR 2012):

$$HQ\ (unitless) = \frac{Exposure\ Point\ air\ Concentration\left(\frac{\mu g}{m3}\right) x\ EF}{Inhalation\ MRL\ or\ RfC\ (\mu g/m3)}$$

So

$$HQ_{RME} = \frac{3.2 \frac{\mu g}{m3} x\ 1}{0.3\ \mu g/m3} = 11$$

Because the HQ exceeds one, health assessors would now conduct additional toxicological evaluation to determine whether non-cancerous harmful effects might be possible.

SCENARIO 2- *Elevated cancer and non-cancer risk*: U.S. EPA requests that ATSDR review data from a facility in KY that produces grinding wheels for commercial use. The most recent Toxic Release Inventory (TRI) facility estimates of emissions are 38 tons per year of total volatile organic material comprised almost completely of naphthalene. Residents live immediately adjacent to the facility on three sides; thus, the perimeter monitors are good surrogates for residential exposure. U.S. EPA conducted sampling in the community over 5 years and gave the health assessor a dataset with the following naphthalene information[6]:

- The naphthalene 5-year average was 6.3 μg/m^3 at the downwind residential location.
- Maximum 1-hour naphthalene averages ranged from 184 – 4,800 μg/m^3.
- 24-hour naphthalene averages ranged from 16 – 1,310 μg/m^3.

Step 1: *Identifying the exposed population*
We know that the community near the site includes children and the elderly, so some people may possibly spend 24 hours of their day being exposed to naphthalene. Since naphthalene is also a carcinogen, our most sensitive chronic endpoint is cancer and our most sensitive population is those who have lived in the community since the facility began operations in 1974. By evaluating facility historical information, we have determined that the operations have remained unchanged since the facility was built and that they have been grandfathered out of environmental regulations for controlling emissions. Naphthalene has not been identified as a mutagen by EPA, so age-dependent adjustment factor calculations are not necessary.

Step 2: *Identifying exposure point concentrations (EPCs)*
Continuous measurements were taken downwind of the stack on the perimeter of the property across the street from residences. We determine the following from the dataset:

- Chronic exposure: Using ATSDR guidance, we identified the 95% UCL of 31.5 μg/m^3 as our upper confidence limit of the mean and chose this value as the chronic EPC.
- Acute exposure: We know that *the 24-hr naphthalene concentrations* ranged from 16 - 1,310 μg/m^3. Using ATSDR EPC guidance, we have established that the acute EPC is 1,180 μg/m^3.

[6] Often, VOC data are provided in units of parts per billion (ppb). To convert ppb to μg/m^3 = (ppb value) * (molecular weight) / (24.45), assuming a temperature of 25°C (77°F) and a pressure of 1 atmosphere (760 mm Hg).

Step 3: *Exposure factor adjustments*
According to ATSDR guidance, the health assessor should assume residents are exposed 24 hours a day, 7 days a week, 52.14 weeks a year (EF = 1). Note that in the residential non-cancer scenario, the CTE and RME exposure factors are identical.
Because the company has been in business since 1974 and we know this community is very stable with many longtime residents, we can make a site-specific assumption that for some residents, chronic exposures have occurred since the facility opened 43 years ago, in lieu of default EFs listed in Section 4.2. Since this is a constant residential exposure scenario, no exposure factor adjustment is needed for non-cancer hazard (the EPC is multiplied by an EF of 1). The exposure factors for this dataset are as follows:

$$\textit{Non-cancer } EF_{chronic} = \frac{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 1\,yr}{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 1\,yr} = 1$$

$$\textit{Cancer } EF_{site\ specific,\ chronic} = \frac{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 43\,yr}{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 78\,yr} = 0.55$$

$$\textit{Non-cancer } EF_{acute} = 24\ hr / 24\ hr = 1$$

Step 4: *Calculating chronic risk for the most sensitive person in the population at risk*

Non-cancer:
For the calculation of non-cancer hazard, we can multiply the annual exposure concentration adjusted to either a CTE or RME duration (both have an EF = 1 in non-cancer residential scenarios) and compare it to the current chronic ATSDR inhalation MRL for naphthalene of 3.7 µg/m^3, yielding a hazard quotient for residential exposure (ATSDR 2005b):

$$HQ\ (unitless) = \frac{Exposure\ Point\ air\ Concentration\ (\mu g/m3)\ x\ EF}{Inhalation\ MRL\ or\ RfC\ (\mu g/m3)}$$

therefore

$$Chronic\ HQ_{RME} = \frac{31.5\ \mu g/m3 * 1}{3.7\ \mu g/m3} = 8.5$$

ATSDR does not currently have an acute or intermediate MRL for naphthalene. Thus, the health assessor should also explore the availability of acute health-based guidelines from state agencies or international health agencies (such as the World Health Organization). Further, the health assessor should evaluate acute exposures by comparing the EPC concentration and the maximum exposures reported in the dataset with health effects reported in the epidemiologic and toxicologic literature. These health effects are summarized in ATSDR's Toxicological Profile for Naphthalene, 1-Methylnapthalene, and 2-Methylnapthalene.
Cancer:

For the calculation of cancer risk, we can multiply the EPC by the U.S. EPA inhalation unit risk (IUR) of 0.000034 µg/m^3 to calculate a cancer risk for our most exposed population using the following equation (U.S. EPA 2020):

$$\textit{Cancer risk} = IUR\ (\mu g/m^3)^{-1} \times \textit{air concentration}\ (\mu g/m^3) \times EF$$

Since we have calculated the EF at 0.55 based on a possible 43 years of exposure, this equation is

$$\textit{Cancer Risk}_{\textit{site-specific RME}} = 0.000034\ (\mu g/m^3)^{-1} \times 31.5\ \mu g/m^3 \times \frac{24\frac{hr}{d} \times 7\frac{d}{wk} \times 52.14\frac{wk}{yr} \times 43\ yr}{24\frac{hr}{d} \times 7\frac{d}{wk} \times 52.14\frac{wk}{yr} \times 78\ yr} = 6.1 \times 10^{-4}$$

The calculated cancer risk of 6.1×10^{-4} means that for every 10,000 persons similarly exposed, 6 extra cases of cancer might be expected. Cancer risks for ATSDR standard age groups can be calculated using age-specific durations for each group.

SCENARIO 3- *Benzene exposure with elevated physical activity*: In this scenario, we will assume a high school is across the street from an asphalt plant emitting uncontrolled benzene from their kiln dryer. The school gym and sports fields are in the predominant downwind direction from the plant, and residents perceive a high rate of leukemia in the school. Given the level of concern from parents of student athletes, **ATSDR was requested to evaluate risk to athletes separately in addition to the rest of the student body**. The sports teams, comprised of juniors and seniors aged 16-18 years, practice three times a week for 2.5 hours each practice day. Inhalation rates for high-school-aged children are presented in Appendix A, Table A-1; the heavy intensity inhalation rate for these athletes is assumed to be 0.049 m^3/min. Exposure during heavy intensity inhalation is assumed to occur for 2.5 hours each practice day, and the long-term default daily inhalation rate for this age range is reported to be 16.3 m^3/day (EFH, 2011; Table 6). Adjusting the exposure frequency for 2.5 hours of heavy intensity respiration and 21.5 hours of "normal" respiration yields:

Passive daily inhalation rate for 16- to 18-year-old high school students: 0.0053 m^3/min (Table A-1); heavy intensity inhalation rates for this same age group is 0.049 m^3/min

- The ventilation volume for 2.5 hours (150 min) under light intensity (school class) conditions for athletes aged 16 to <21 is $\underline{1.80\ m^3}$ (150 min x 0.012 m^3/min)
- The ventilation volume for 2.5 hours (150 min) under high intensity activity conditions is $\underline{7.35\ m^3}$ (150 min x 0.049 m^3/min)

This means that under high intensity activity scenarios and assuming dose linearity, the students breathed four times more air (with an exposure level of approximately four times more), increasing their risk by this ratio for their acute exposure time of 2.5 hours. If these students also attend a school exposed to emissions, exposure during the school day should be evaluated (see RME and CTE exposure factors in Tables 3 and 4).
Risk from each time period would then be summed to give an overall risk for the students during their time at the school affected by facility emissions. In this case, the hazard quotient and cancer risk are influenced not only by the exposure factor, but also by the heavy intensity activity for athletes and light intensity activity for all students. The hazard quotient, calculated for the

practice duration as well as the school day, is summed for total risk for the most at-risk population—student athletes.

The steps to this assessment are outlined below:

Step 1: *Identifying the exposed population*
We know that high school juniors and seniors are exposed 2.5 hours each practice day (i.e., 3 days a week.) We also assume those same students are exposed to emissions from the asphalt plant during their school day.

Step 2: *Identifying exposure point concentrations (EPCs)*
Continuous measurements were collected on school property, across from the asphalt plant. We determine the following from the dataset:

- Chronic exposure: Using ATSDR EPC guidance, we identify a chronic benzene EPC of 2.3 ppb (7.3 µg/m^3).
- Acute exposure: Using ATSDR EPC guidance, continuous benzene measurements indicate a 1-hour EPC is 25 ppb (79.9 µg/m^3).

Step 3: *Exposure factor adjustments*
We are calculating exposures for the student athletes during practice as well as all students who attend the school affected by the facility. We will use RME assumptions to be protective of the athletes (2.5 hours of practice, 3 days a week) and of students who spend the maximum amount of time at school (Per Table 3, this age group's RME school day is 9.6 hours (we are assuming 2.5 hours for practice and 7.1 hours for classes). The exposure factor calculation for our 2-year dataset is as follows:

<u>Outdoor practice exposure factors</u> (2.5 hr/3 day a week over a school year) assuming short-term heavy intensity inhalation rate over the default light intensity breathing rate from Appendix A:

$$Non\text{-}cancer\ EF_{chronic} = \left(\frac{0.049\ m3/min}{0.012\ m3/min}\right)\ x\ \frac{2.5\,\frac{hr}{d}\ x\ 3\,\frac{d}{wk}\ x\ 39\,\frac{wk}{yr}\ x\ 2\ yr}{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 2\ yr} = 0.14$$

$$Non\text{-}cancer\ EF_{acute} = \left(\frac{0.049\ m3/min}{0.012\ m3/min}\right)\ x\ 2.5\ hr\ /\ 24\ hr = 0.43$$

$$Cancer\ EF_{chronic} = \left(\frac{0.049\ m3/min}{0.012\ m3/min}\right)\ x\ \frac{2.5\,\frac{hr}{d}\ x\ 3\,\frac{d}{wk}\ x\ 39\,\frac{wk}{yr}\ x\ 2\ yr}{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 78\ yr} = 0.0035$$

<u>School day exposure factors</u> (EFs) assuming short-term default light intensity inhalation rates from Appendix A:

$$RME\ Non\text{-}cancer\ EF_{chronic} = \left(\frac{0.012\ m3/min}{0.012\ m3/min}\right)\ x\ \frac{7.1\,\frac{hr}{d}\ x\ 5\,\frac{d}{wk}\ x\ 39\,\frac{wk}{yr}\ x\ 2\ yr}{24\,\frac{hr}{d}\ x\ 7\,\frac{d}{wk}\ x\ 52.14\,\frac{wk}{yr}\ x\ 2\ yr} = 0.16$$

$$Non\text{-}cancer\ EF_{acute} = \left(\frac{0.012\ m3/min}{0.012\ m3/min}\right)\ x\ 7.1\ hr\ /\ 24\ hr = 0.30$$

$$Cancer\ EF_{chronic} = \left(\frac{0.012\ m3/min}{0.012\ m3/min}\right)\ x\ \frac{7.1\frac{hr}{d}\ x\ 5\frac{d}{wk}\ x\ 39\frac{wk}{yr}\ x\ 2\ yr}{24\frac{hr}{d}\ x\ 7\frac{d}{wk}\ x\ 52.14\frac{wk}{yr}\ x\ 78\ yr} = 0.0040$$

Step 4: *Calculating Risk*

Non-cancer, chronic exposure

We can use the HQ_{adj} Formulas on pages 32-33 to adjust the exposure factors for student athletes and school day exposure with the heavy intensity activity and default breathing rate ratio.

Chronic risk during outdoor practice (2.5 hrs/3 days per week, heavy intensity breathing rate):

$$Outdoor\ practice\ HQ_{chronic} = \frac{EPC}{Inhalation\ MRL} * EF_{chronic,\ non-cancer} = \left(\frac{2.3\ ppb}{3\ ppb}\right) * 0.14 = \mathbf{0.10}$$

Chronic risk during the regular school day (RME duration, hrs/days per week, normal breathing rate):

$$Student\ chronic\ HQ_{chronic} = \frac{EPC}{Inhalation\ MRL} * EF_{chronic,\ non-cancer} = \left(\frac{2.3\ ppb}{3\ ppb}\right) * 0.16 = \mathbf{0.12}$$

The total school day risk is the sum of these two adjusted HQs for the most exposed students (the student athletes):

***Total chronic HQ for student athletes (non-cancer)* = 0.10 + 0.12 = 0.22**

Non-cancer, acute exposure

For the calculation of acute non-cancer hazard, we can adjust the exposure by using the acute EPC (25 ppb), multiplying by the breathing rate ratio and the acute exposure factor, then calculating a hazard quotient of the ratio of the adjusted EPC to the current acute ATSDR inhalation MRL for benzene of 9 ppb using the equations below.

Acute risk during outdoor practice (2.5 hrs/3 days per week, heavy intensity breathing rate):

$$Outdoor\ practice\ HQ_{acute} = \frac{EPC}{Inhalation\ MRL} * EF_{acute,\ non-cancer} = \left(\frac{25\ ppb}{9\ ppb}\right) * 0.43 = \mathbf{1.2}$$

<u>Acute risk during the regular school day</u> (RME duration, normal breathing rate):

$$Student\ acute\ HQ_{\text{acute}} = \frac{EPC}{Inhalation\ MRL} * EF_{acute,\ non-cancer} = \left(\frac{25\ ppb}{9\ ppb}\right) * 0.30 = \mathbf{0.83}$$

The total school day non-cancer hazard is the sum of these two adjusted HQs for the most exposed students (the student athletes):

Total acute HQ for student athletes **= 1.2 + 0.83 = <u>2.0</u>**

<u>Cancer, chronic exposure</u>

For the calculation of cancer risk, we multiply the heavy intensity activity and default breathing rate ratio by the EPC and the U.S. EPA inhalation unit risk (IUR) of 0.0000078 $(\mu g/m^3)^{-1}$ using the following equation (*Note: for this example, the air concentration of 2.3 ppb was converted to 7.3 $\mu g/m^3$ for consistency with the IUR units)*:

Cancer risk = IUR x EPC $(\mu g/m^3)$ *x EF*

Since we have calculated the EF (0.0035) based on 2 years of exposure over a lifetime, we can calculate the additional cancer risk during outdoor practice using the following equation:

Outdoor practice cancer risk $= 0.0000078\ (\mu g/m^3)^{-1} * 7.3\ \mu g/m^3 * 0.0035 = \mathbf{2.0*10^{-7}}$

Similarly, we can use the RME EF of student exposure based on 2 years of exposure over a lifetime (0.004) to calculate the additional cancer risk during the regular school day using the following equation:

Student cancer risk $= 0.0000078\ (\mu g/m^3)^{-1} * 7.3\ \mu g/m^3 * 0.004 = \mathbf{2.3*10^{-7}}$

Total school day cancer risk is the sum of these two adjusted cancer risks for the most exposed students (the football players):

Total cancer risk for school day = **$2.0*10^{-7}$ (outdoor practice) + 2.3×10^{-7} (school day) = <u>4.3×10^{-7}</u>**