

The recommended approach for estimating excess cancer risk from exposure via multiple routes is to first estimate cancer risk from each exposure pathway and then sum across the multiple routes.⁴⁰

For the effects assessed via a reference value, risk assessors should calculate the HI for each exposure pathway and sum across the multiple routes. Separate total HIs should be calculated for each type of exposure period (i.e., chronic, subchronic or acute). If the HI exceeds one, there may be concern for potential adverse effects and risk assessors should consider deriving separate HIs for each target organ of concern.

9. RISK CHARACTERIZATION

Risk characterization is the final, summarizing step in conducting a risk assessment. Generally, the purpose of the risk characterization section of a report is to:⁴¹

- Describe the key findings of the risk assessment in a transparent manner, including identifying hazard, characterizing the dose-response relationship, and describing receptor exposures;
- Identify and describe the scientific and policy assumptions used in the assessment;
- Characterize uncertainties in results; and
- Provide an overall conclusion about the risks present at a site (USEPA, 2000c).

A well-crafted risk characterization section puts risk calculations into context for risk managers so that they may effectively weigh and interpret risk assessment results (i.e., it is the interface between risk assessment and risk management). A few of the key issues and uncertainties involved in calculating risks from inhalation exposures are outlined below.

9.1 Highly Exposed or Susceptible Populations and Life Stages

EPA recommends that the risk characterization portion of the risk assessment explain any particular susceptibilities to inhaled toxicants or potential for increased inhalation exposures among the various receptor groups at a site.⁴² We discuss below two possible examples, children and worker receptors, though this discussion could apply to other receptor characteristics as well (e.g., age, disease, gender, genetic characteristics).

9.1.1 Children

One population group that could potentially be more highly exposed to inhalation exposures at a site is children. As discussed in Section 6.2, exposure parameters related to activity patterns (e.g., exposure time, frequency, and duration) and MEs, may vary across age groups. For example, due to outdoor play patterns, children may spend more time near the source of contamination than adults,

⁴⁰Note that this approach is generally most appropriate for total cancer risks of less than 0.1 (EPA, 1989).

⁴¹For specific information on the format of risk characterizations, refer to *Elements to Consider when Drafting EPA Risk Characterizations* (EPA, 1995c).

⁴²EPA's IRIS glossary defines susceptibility as the following: "Increased likelihood of an adverse effect, often discussed in terms of relationship to a factor that can be used to describe a human subpopulation (e.g., life stage, demographic feature, or genetic characteristic)" (EPA, 2008b).

and thus would have higher exposure time and/or exposure frequency values than adults living in the same location. Therefore, it is important to carefully describe site-specific exposures to children, and assumptions made in risk calculations.⁴³

If chemical-specific data on susceptibility to the toxic effects from early life exposures are available, these data are considered when developing toxicity values that specifically address differential toxicity to the young (e.g., vinyl chloride) (USEPA, 2005c). Toxicity values derived using the default approach from the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive subgroups. Therefore, as described in Section 6 of Appendix A, no quantitative adjustment of toxicity values derived using the default approach in the *Inhalation Dosimetry Methodology* is recommended for specific age groups to account for different ventilation rates or body weights of specific age groups.

When evaluating risk to carcinogenic chemicals with a demonstrated mutagenic MOA but which lack chemical-specific information on susceptibility from early life exposures, EPA recommends a quantitative adjustment of the toxicity value to account for early life susceptibility, as described in the *Supplemental Cancer Guidelines* (see USEPA, 2005b & 2005c; and Section 5.1 of this guidance for further information).

9.1.2 Workers

Workers could have increased exposure under certain occupational scenarios. Some outdoor workers might spend more time near a source of contamination in the course of their job and this should be reflected in adjustments to the exposure parameters (e.g., ET, Exposure Frequency (EF), and ED) describing the worker exposure scenario. Toxicity values derived using the *Inhalation Dosimetry Methodology* are developed for the human population as a whole, including sensitive populations and life stages. In the default *Inhalation Dosimetry Methodology* approach, typical variation in IRs between periods of high activity and rest is considered. However, if workers have especially high levels of exertion with correspondingly high ventilation rates, these workers could be at the upper end of the risk range, particularly if they are exposed to Category 1 gases, which have direct effects in the respiratory tract. This implication should be recognized in the risk characterization section.

9.2 Uncertainties in Inhalation Risk Assessment

This guidance recommends including an assessment of the key uncertainties that may significantly impact risk estimates for inhaled chemicals. This should ensure transparency, clarity, reasonableness and consistency in risk assessments, as recommended by EPA's *Policy for Risk Characterization* (USEPA, 1995a). Other sources of uncertainty may be present and other EPA documents provide guidance on characterizing uncertainty in risk the assessment process (USEPA, 1992, 1995a, 1995b, 1995c, 1997a, 1997b). Key uncertainties related to inhalation risk assessment, which is the focus of this section, include the development of ECs, choice of toxicity value, lack of quantitative toxicity information via inhalation, and the approach to estimating and aggregating risks. According to EPA's *Guidance for Risk Characterization*, the discussion of uncertainty "should reflect the type and complexity of the risk assessment, with the level of effort for analysis and discussion of uncertainty

⁴³ For additional information on children's health risk assessment, please consult *A Framework for Assessing Health Risks of Environmental Exposures to Children* (EPA, 2006b).

corresponding to the level of effort for the assessment” (USEPA, 1995b). Therefore, risk assessors should provide a qualitative and/or quantitative evaluation of key uncertainties pertaining to inhalation risk, and their impact on the outcome of the assessment, consistent with the level of effort of the specific risk assessment.

9.2.1 Development of Exposure Concentrations

As described in Section 3 of this guidance, with the exception of acute exposures, time-weighted averages are typically used to represent intermittent or variable inhalation exposures to receptors at a site. This recommended approach is consistent with the duration adjustment approach (based on Haber’s Law) that is generally used in deriving the toxicity values (see Section 2.1.1.1 for further information). As mentioned in Section 3, when evaluating situations in which the exposure is long-term, yet there are short periods of significantly higher exposure, those periods should also be assessed using appropriate short-term toxicity values. This ensures that periods of much higher exposure can be appropriately assessed and not “diluted out” in the assessment of longer-term exposure.

When information on multiple MEs exists at a site, risk assessors may choose to estimate ECs as outlined in Section 3.4. However, this typically requires sufficient time-activity information of receptors at a site to accurately determine the time spent in each ME. Incomplete or low quality data on time-activity pattern may introduce uncertainty into the estimation of the ECs for MEs. Risk assessors should describe the quality and completeness of these data.

The recommended method for determining the CA at a site can potentially introduce uncertainty into the EC calculations. For instance, if contaminant concentrations in air are measured, risk assessors should consider uncertainties related to how well the set of air samples available at a site represents the duration and time period being assessed as well as measurement uncertainty related to the methods and equipment used. In addition, risk assessors should describe any potential confounding of indoor air samples by other sources of contaminants (e.g., household products). If contaminant concentrations in air are modeled, (e.g., by EPA’s spreadsheet models for vapor intrusion) risk assessors should address model-related uncertainties and their potential impact on the estimate of contaminant concentrations in air. Considerations of particle size at the site versus particle size used to derive the toxicity value are also important.

9.2.2 Toxicity Assessment

Section 4.1 of this document indicates that some IURs on IRIS were developed through extrapolation from oral CSFs (see Appendix B of this document). The use of toxicity values derived through simple route-to-route extrapolation introduces additional uncertainty into risk calculations. Therefore, risk assessors should indicate when extrapolated IURs are used and should characterize the potential impact of the uncertainty associated with using these values, if known.

Section 4.2 and Appendix C of this guidance recommends contacting STSC to help identify appropriate toxicity values for conducting a risk assessment at Superfund sites in the absence of published inhalation toxicity values. If STSC is unable to recommend a toxicity value, risk assessors should acknowledge the resulting uncertainty in risk associated with the chemical(s) lacking inhalation toxicity data. If STSC provides risk assessors with a toxicity value based on a PBPK

model, model uncertainty should be discussed. In addition, if STSC provides risk assessors with one or more structurally analogous chemicals, risk assessors can use toxicity data for these chemicals to help characterize the potential magnitude of the inhalation risk associated with the chemical(s) lacking data. In this case, risk assessors should acknowledge the uncertainty associated with relying on toxicity data for analogous chemicals to characterize risk at the site.

Risk assessors should also acknowledge chemicals that lack duration-appropriate toxicity values and discuss the potential impacts of substituting alternative toxicity values for HQ calculations. For instance, if the ED is determined to be subchronic but no subchronic inhalation RfC or analogous toxicity value is available for that chemical, the risk assessor should address the uncertainty associated with calculating an HQ using a toxicity value for a different duration, such as chronic, or the impact of not quantifying those risks. In addition, if risk assessors use an acute toxicity value that does not match the duration of the acute exposure being assessed, the possibility of under or overestimating hazard should be discussed.

When conducting a screening-level risk assessment using screening values such as those described in Section 7, it is important to further evaluate and clearly describe the quality and uncertainties associated with the inhalation toxicity values used in the risk assessment if measured sample contaminant concentrations at a site exceed these screening values.

9.2.3 Estimating Cancer Risks

For high exposures, for example those within the range of epidemiological studies (usually those predicted to have risks greater than 10^{-2}), the IUR derived from the linear extrapolation below the range of observation is generally not appropriate for use (see Section 5.1 of this document for further information).⁴⁴ Risk assessors should provide specific information in the risk characterization describing how these high exposures were addressed in the risk assessment. For instance, if a risk assessor chose to provide a semi-quantitative approach (e.g., indicating that risks are above 10^{-2}), this should be indicated, along with a description of the uncertainties involved in not fully quantifying risk associated with exposure to this chemical. If a risk assessor chose to use the original model in the IRIS file or other technical background document, the risk characterization section should include a description of any uncertainties in the model used and could contain examples of the risks estimated.

9.2.4 Estimating Risk and Hazard from Multiple Chemicals and Exposure Pathways

Risk assessors should also describe uncertainties involved in aggregating risk and hazard across multiple chemicals and exposure pathways. For instance, the approaches described in Section 8 of this document are associated with several assumptions (e.g., independence of action and doses for individual compounds at levels not expected to be of concern). If these assumptions are not met, aggregation may not be appropriate. This should be fully described in the risk characterization section and any uncertainties involved in the lack of quantitative information should be indicated.

⁴⁴ Also refer to Section 8.2.1 of RAGS, *Part A* for further discussion of this topic (EPA, 1989, page 8-6).