RISK ASSESSMENT GUIDANCE FOR SUPERFUND, PART F:
SUPPLEMENTAL GUIDANCE FOR INHALATION RISK ASSESSMENT

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Topics

- Purpose of the document
- Project history
- Workgroup members
- Comparison of previous and updated inhalation methodologies
- Examples of RAGS F implementation
- FAQs
Purpose of Document

To update and supersede existing Superfund (SF) guidance on calculating cancer and non-cancer risk from contaminant exposures through the inhalation route (e.g., RAGS, Part A) to be consistent with updated science concerning inhalation dosimetry.

Document endorses the use of the Reference Concentration (RfC) and Inhalation Unit Risk (IUR) approach to inhalation risk assessment instead of the use of Inhalation Reference Doses (RfD) and inhalation Cancer Slope Factors (CSF).

Document provides recommendations concerning key issues in inhalation risk assessment (e.g., route-to-route extrapolation).
Project History


- **January 2009** – RAGS F is final. OSWER # 9285.7-82

- **April 2009** – Regional Screening Level Table incorporates RAGS F methodologies.
Workgroup Members

- Dave Crawford (OSWER/OSRTI)*
- Michael Sivak (Region 2)*
- Brenda Foos (OCHP)
- Gary Foureman (ORD/NCEA)
- Ann Johnson (OA/OPEI)
- Deirdre Murphy (OAR/AQPS)
- Arunas Draugelis (Region 5)
- Cheryl Overstreet (Region 6)
- Jeremy Johnson (Region 7)
- Bob Benson (Region 8)
- Susan Griffin (Region 8)
- Daniel Stralka (Region 9)
- Marcia Bailey (Region 10)
- Tyra Walsh (IEc)
- Henry Roman (IEc)
- Erik Ruder (IEc)

- Sarah Levinson (Region 1)
- Jennifer Hubbard (Region 3)
- Ofia Hodoh (Region 4)
- Kevin Koporec (Region 4)
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- Cheryl Overstreet (Region 6)
- Jeremy Johnson (Region 7)
- Bob Benson (Region 8)
- Susan Griffin (Region 8)
- Daniel Stralka (Region 9)
- Marcia Bailey (Region 10)
- Tyra Walsh (IEc)
- Henry Roman (IEc)
- Erik Ruder (IEc)

* Co-chair
Previous Approach Compared to Updated Approach: Carcinogens

**Previous Approach (RAGS, Part A):**
Chronic Daily Intake = CA x (IR/BW) x (ET x EF x ED)/AT
Cancer Risk = Intake x CSF$_i$

**Updated Approach (1994 Guidance):**
Exposure Concentration (EC) = (CA x ET x EF x ED)/AT
Cancer Risk = EC x IUR

Where: CA = concentration in air; IR = Inhalation Rate; BW = bodyweight; ET = exposure time; EF = exposure frequency; ED = exposure duration; AT = averaging time; CSF$_i$ = inhalation cancer slope factor; and IUR = inhalation unit risk.
Previous Approach Compared to Updated Approach: Non-Carcinogens

**Previous Approach (RAGS, Part A):**
Chronic Daily Intake = CA × (IR/BW) × (ET × EF × ED)/AT
Hazard Quotient (HQ) = Intake/RfD_i

**Updated Approach (1994 Guidance):***
Exposure Concentration (EC) = (CA × ET × EF × ED)/AT
HQ = EC/RfC

Where: CA = concentration in air; IR = Inhalation Rate; BW = bodyweight; ET = exposure time; EF = exposure frequency; ED = exposure duration; AT = averaging time; RfD_i = inhalation reference dose; and RfC = reference concentration.

* = this example assumes a chronic exposure scenario
Exposure Scenario Examples

- Hypothetical site contaminated with Benzene
- Residential and Commercial/Industrial (chronic)
  - Chronic CA = 100 µg/m³
  - IUR from IRIS = Range from 2.2E-6 to 7.8E-6 per µg/m³
  - RfC from IRIS = 3E-2 mg/m³ = 30 µg/m³
- Trespasser (intermittent)
Residential Exposure Scenario Example

Cancer Risk:
EC = \( [CA \times ET \times EF \times ED]/AT \)
EC = \( [100 \, \mu g/m^3 \times 24 \, h/d \times 350 \, d/y \times 30 \, y]/[70 \, y \times 24 \, h/d \times 365 \, d/y] \)
EC = 41 \, \mu g/m^3
Cancer Risk = EC \times IUR = 41 \, \mu g/m^3 \times 7.8E-6 = 3.2E-4

Non-Cancer Hazard:
EC = \( [CA \times ET \times EF \times ED]/AT \)
EC = \( [100 \, \mu g/m^3 \times 24 \, h/d \times 350 \, d/y \times 30 \, y]/[30 \, y \times 24 \, h/d \times 365 \, d/y] \)
EC = 96 \, \mu g/m^3
HQ = EC/RfC = 96 \, \mu g/m^3/30 \, \mu g/m^3 = 3.2
Commercial/Industrial Exposure Scenario Example

Cancer Risk:
EC = \([CA \times ET \times EF \times ED]/AT\)
EC = \([100 \ \mu g/m^3 \times 8 \ h/d \times 250 \ d/y \times 25 \ y]/[70 \ y \times 24 \ h/d \times 365 \ d/y]\)
EC = 8.2 \ \mu g/m^3
Cancer Risk = EC × IUR = 8.2 \ \mu g/m^3 \times 7.8E-6 = 6.4E-5

Non-Cancer Hazard:
EC = \([CA \times ET \times EF \times ED]/AT\)
EC = \([100 \ \mu g/m^3 \times 8 \ h/d \times 250 \ d/y \times 25 \ y]/[25 \ y \times 24 \ h/d \times 365 \ d/y]\)
EC = 23 \ \mu g/m^3
HQ = EC/RfC = 23 \ \mu g/m^3/30 \ \mu g/m^3 = 0.8
FIGURE 2
RECOMMENDED PROCEDURE FOR DERIVING EXPOSURE CONCENTRATIONS AND HAZARD QUOTIENTS FOR INHALATION EXPOSURE SCENARIOS

Step 1: Assess Duration

Acute
(e.g., minutes/hours to days)*

Subchronic
(e.g., weeks to years)*

Chronic
(e.g., many years)*

Step 2: Assess Exposure Pattern

Is the duration of the exposure scenarios generally acute, subchronic, or chronic?

Subchronic
(e.g., weeks to years)*

Are there 1 or more periods of exposure, each of which is generally as frequent as a subchronic toxicity test (e.g., 6-8 hrs/day, 5 days/wk)?*

Yes

No

Calculate acute EC & HQs for each acute exposure period
Equation 7
Equation 12
[Repeat for each chemical]

Calculate subchronic EC & HQs for each subchronic exposure period
Equation 8
Equation 12
[Repeat for each chemical]

Calculate chronic EC & HQ
Equation 8
Equation 12
[Repeat for each chemical]

Step 3: Estimate EC

Is the EF generally as frequent as a chronic toxicity test or an occupational study (e.g., 6-8 hrs/day, 5 days/wk, 50 wks/yr)?†

Yes

No

* The specific definition for each duration category may vary depending on the source of the toxicity value being used. For Tier 1 toxicity values obtained from IRIS:
  acute exposures are defined as those lasting 24 hours or less;
  subchronic exposures are defined as repeated exposures for more than 30 days, up to approximately 10 percent of the life span in humans; and
  chronic exposures are defined as repeated exposures for more than approximately 10 percent of the life span in humans (EPA, 2008).

† For the purposes of this document, short-term exposures, defined by the IRIS glossary as repeated exposures for more than 24 hours, up to 30 days, should be treated as subchronic.

‡ Exposure regimens vary from study to study. Risk assessors should use best professional judgment to determine if the exposure pattern in a given scenario is reasonably similar to a typical regimen for a chronic or subchronic study.
Trespasser Exposure Scenario Example

- Acute CAs = 1-h samples: 200 µg/m³, 120 µg/m³, 95 µg/m³; 8-h samples: 80 µg/m³, 100 µg/m³, 110 µg/m³
- CalEPA Acute Reference Exposure Level (REL) = 1,300 µg/m³ (based on 6-h exposure)
Trespasser Exposure Scenario Example (Cont.)

**Cancer Risk:**
EC = \([CA \times ET \times EF \times ED]/AT\)
EC = \([100 \, \mu g/m^3 \times 2 \, h/d \times 100 \, d/y \times 2 \, y]/[70 \, y \times 24 \, h/d \times 365 \, d/y]\)
EC = 0.07 \, \mu g/m^3
Cancer Risk = EC \times IUR = 0.07 \, \mu g/m^3 \times 7.8E-6 = 5.5E-7

**Non-Cancer Hazard:**
EC = CA (for each acute exposure period)
EC = 200 \, \mu g/m^3 OR 110 \, \mu g/m^3
HQ = \frac{EC}{REL_{acute}} = \frac{200 \, \mu g/m^3}{1,300 \mu g/m^3} = 0.15 OR
\quad = \frac{110 \, \mu g/m^3}{1,300 \mu g/m^3} = 0.09
<table>
<thead>
<tr>
<th>Chemical of Potential Concern</th>
<th>Chronic/ Subchronic</th>
<th>Inhalation RfC</th>
<th>Extrapolated RfD</th>
<th>Primary Target Organ(s)</th>
<th>Combined Uncertainty/Modifying Factors</th>
<th>RFC : Target Organ(s)</th>
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</thead>
<tbody>
<tr>
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<td>Units</td>
<td>Value</td>
<td>Units</td>
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<td>NA</td>
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<td>Nasal</td>
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<td>NCEA</td>
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<tr>
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<td>100</td>
<td>NCEA</td>
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</tr>
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<td>mg/m3</td>
<td>CNS</td>
<td>300</td>
<td>NCEA</td>
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<td>Barium</td>
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<td>mg/m3</td>
<td>Fetus</td>
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<td>Subchronic</td>
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<td>mg/m3</td>
<td>Fetus</td>
<td>100</td>
<td>HEAST</td>
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<tr>
<td>Manganese (nonfood)</td>
<td>Chronic</td>
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<td>mg/m3</td>
<td>CNS</td>
<td>1000</td>
<td>IRIS</td>
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</tbody>
</table>

Definitions: NA = Not Available
IRIS = Integrated Risk Information System
HEAST = Health Effects Assessment Summary Table, July 1997
NCEA = National Center for Environmental Assessment
TABLE 6.2
CANCER TOXICITY DATA – INHALATION
The Dean Company

<table>
<thead>
<tr>
<th>Chemical of Potential Concern</th>
<th>Unit Risk</th>
<th>Inhalation Cancer Slope Factor</th>
<th>Weight of Evidence/ Cancer Guideline Description</th>
<th>Unit Risk : Inhalation CSF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Value</td>
<td>Value</td>
<td>Units</td>
<td>Source(s) Date(s) (MM/DD/YYYY)</td>
</tr>
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<td>NA</td>
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<td>NA</td>
</tr>
<tr>
<td>4,4'-DDE</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>4,4'-DDT</td>
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<td>1/ug/m3</td>
<td>B2 - IRIS</td>
<td>06/21/01</td>
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<tr>
<td>Bis(2-ethylhexyl)phthalate</td>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Chloroform</td>
<td>2.3E-05</td>
<td>1/ug/m3</td>
<td>B2 - IRIS</td>
<td>06/21/01</td>
</tr>
<tr>
<td>Heptachlor</td>
<td>1.3E-03</td>
<td>1/ug/m3</td>
<td>B2 - IRIS</td>
<td>06/21/01</td>
</tr>
<tr>
<td>Aluminum</td>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
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<td>Lead</td>
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<tr>
<td>Manganese (nonfood)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Definitions:
NA = Not Available
IRIS = Integrated Risk Information System
B2 = Probably Human Carcinogen - indicates sufficient evidence in animals and inadequate or no evidence in humans
Inhalation Screening Levels

- RAGS F provides equations for calculating target contaminant concentrations in air.
- RAGS F also discusses target concentrations in other media, such as soil, tap water, and soil gas or ground water values for vapor intrusion.
### TABLE 4
RECOMMENDED PROCEDURE FOR CALCULATING RISK-BASED SCREENING CONCENTRATIONS FOR CONTAMINANTS IN AIR

<table>
<thead>
<tr>
<th>Step 1: Select Target Levels</th>
<th>Cancer Risk-Based</th>
<th>Hazard-Based&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Select target cancer risk (e.g., 1 x 10^-6).</td>
<td>Select target HQ (e.g., 1).</td>
<td></td>
</tr>
</tbody>
</table>

| Step 2: Identify Toxicity Value<sup>2</sup> | Identify inhalation cancer potency value (e.g., IUR). If none exists, proceed with hazard-based screening level calculation. | Identify inhalation reference value (e.g., RfC) to match exposure scenario (acute, subchronic, chronic). If none exist, proceed with cancer screening level calculation. |

| Step 3: Calculate CA | Using target cancer risk from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target Risk)/(IUR x ET x EF x ED) | Using target HQ from Step 1 along with the receptor- and scenario-specific exposure parameter values, calculate CA; the following equation is recommended: CA = (AT x Target HQ x RfC x 1000 µg/mg)/(ET x EF x ED) |

| Step 4: Select Screening Concentration | Select minimum of predicted cancer risk- and hazard-based values as screening concentrations. Repeat for each receptor/scenario combination of interest. | |

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<sup>1</sup> Hazard-Based risk assessment

<sup>2</sup> For cancer risk assessment, this step is not applicable.

<sup>3</sup> Repeat for each receptor/scenario combination of interest.
FAQ: Inhalation Risk Assessment for Children

- Application of Age-Dependant Adjustment Factors (ADAFs) recommended for chemicals with a mutagenic mode of action (MMOA) if no child-specific IUR exists on IRIS or PPRTV (per the Supplemental Cancer Guidelines).
- No other adjustments to inhalation toxicity values recommended when assessing risk to children.
- Activity patterns for children may differ, potentially leading to higher exposures (e.g., outdoor play). This will be addressed as part of the exposure assessment and reflected in the calculations of the EC.
As part of the risk characterization process, risk assessors can identify site-specific subpopulation sensitivities.

RAGS F presents a comparison of a Human Equivalent Concentration (HEC) calculated with the EPA default parameters with HECs calculated using age- and activity group-specific parameters (Appendix A).
FAQ: Availability of Inhalation Toxicity Values

- RAGS F discourages risk assessors from performing route-to-route extrapolation using default body weight and inhalation rate parameters.
- RAGS F recommends risk assessors contact NCEA’s Superfund Health Risk Technical Support Center (STSC) to pursue an alternate value through PBPK modeling or a surrogate chemical for SF site analyses.
- If no alternate value is available, document recommends performing a qualitative risk assessment, noting the lack of information in the uncertainty section.
FAQ: Availability of Inhalation Toxicity Values (Cont.)

- Regional Screening Levels for Chemical Contaminants at Superfund Sites as of December 2008
  - 134 RfCs
  - 138 IURs

- IRIS
  - 72 RfCs
  - 54 IURs
In Summary

- RAGS F updates equations to calculate risk/hazard to account for dosimetry used in the toxicity derivation.
- Population-specific adjustments such as body weight and inhalation rate are no longer needed in the exposure since they are incorporated into the toxicity.
- Important to identify appropriate exposure duration so that the correct RfC is used.
- Do not adjust oral toxicity values using inhalation rates and body weights.
- Risk characterization should identify population susceptibilities and potential underestimation of risk from chemicals for which no RfCs/IURs are available.