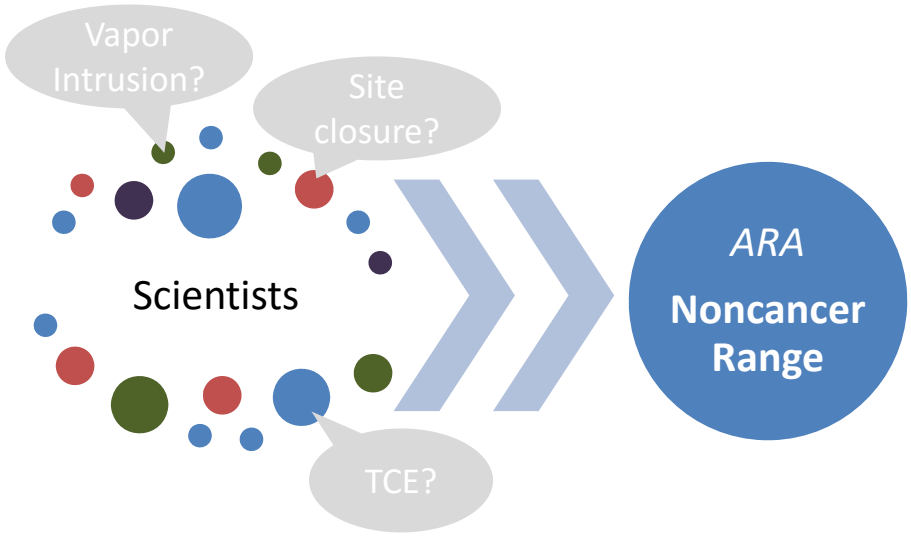
Alliance for Risk Assessment (*ARA*)



Purpose: Guidance for Noncancer Range at Contaminated Sites

- Develop a range in noncancer risks, similar to the range used for cancer risks in management of waste sites, using readily available information from U.S. EPA and elsewhere.
- Create range to enable evaluation of uncertainty in the noncancer benchmark.
- Demonstrate confidence in this range so that the range can be considered in the determination of management choices.

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Practical Guidance for Contaminated Sites:
Trichloroethylene (TCE) Case Study Webcast

– Ed Pfau, HULL & Associates
– Oliver Kroner, Alliance for Risk Assessment
– Rod Thompson, Alliance for Site Closures
– Tania Onica, Ontario Ministry of the Environment
– Helen Dawson (recently EPA), now Geosyntec
– Lenny Siegel, Center for Public Environmental Oversight
– David Gillay, Barnes & Thornburg LLP
– Michael Dourson, Toxicology Excellence for Risk Assessment
– Calvin C. Willhite, Risk Sciences International
– Edward W. Carney, The Dow Chemical Company
– Linval R. DePass, Durect Corporation in Cupertino
– Stephen B. Harris, Stephen B. Harris Group
– Melissa Marr, RTI International

Developing the Range

An RfC is an estimate (with uncertainty spanning perhaps an **order of magnitude**) of a **daily oral** (for RfD) **or continuous** inhalation (for RfC) exposure to the human population (including **sensitive** subgroups) that is **likely to be without** an appreciable risk of deleterious effects during a lifetime.

- Arsenic RfD on IRIS.
  - There was not a clear consensus among Agency scientists on the oral RfD. Applying the Agency's RfD methodology, strong scientific arguments can be made for various values within a factor of 2 or 3 of the currently recommended RfD value, i.e., 0.1 to 0.8 ug/kg/day. It should be noted, however, that the RfD methodology, by definition, yields a number with inherent uncertainty spanning perhaps an order of magnitude.

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Developing the Range (con't)

- In the IRIS Summary for TCE, U.S. EPA identified three RfC values for the noncancer inhalation toxicity of TCE. These are:
  - RfC of 2 µg/m^3 based on decreased thymus weight in female mice (Keil *et al.*, 2009);
  - RfC of 2 µg/m^3 based on fetal heart malformations in rats (Johnson *et al.*, 2003); and
  - RfC of 3 µg/m^3, based on toxic nephropathy in female rats (NTP, 1988).
- Each of these RfCs may be evaluated with respect to the imprecision and the uncertainty inherent in its derivation.

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Different Uncertainty Ranges for TCE RfCs

Table 7. Different uncertainty ranges for different TCE RfCs. All values are in µg/m^3. Shaded areas indicate best **overall uncertainty range** for risk management purposes.

Study	IRIS UF [a]	Steep [b] Slope	Confidence		Uncertainty Ranges		
			Critical [c] Effect	Point of [d] Departure	Floor	Intermediate	Ceiling
Johnson et al (2003)	10	Lower	Low	Low	2	10	20
NTP (1988)	10	Higher	Medium	Medium to Low	3	9	30
Keil et al. 2009	100	NA	Medium	Medium to Low	2	20	190

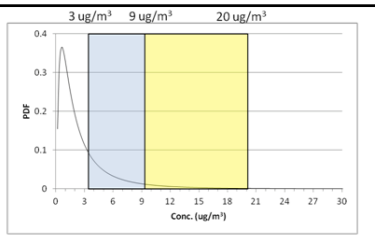

Figure 3a. Exposure distribution of indoor air concentrations primarily below the 3 µg/m3 to 20 µg/m3 hazard range. Relatively small proportion of exposures is higher than 3 µg/m3. Nominal actions or no further action may be warranted for risk management.

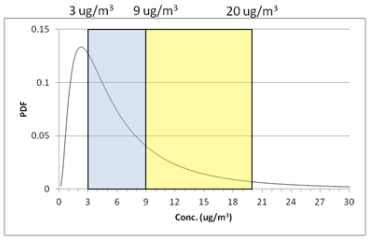

Figure 3b. Exposure distribution of indoor air concentrations falling within the 3 µg/m3 to 20 µg/m3 hazard range. Relatively small proportion of exposures is higher than 9 µg/m3. Limited action may be warranted for risk management.

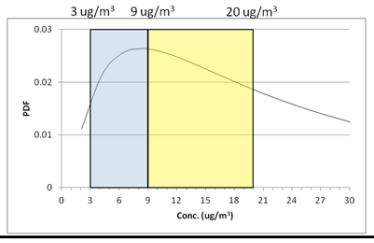

Figure 3c. Exposure distribution of indoor air concentrations primarily above the 3 µg/m3 to 20 µg/m3 hazard range. Actions to reduce exposures may be warranted for risk management.

Summary: Noncancer Range at Contaminated Sites

- A general range was developed for noncancer risk values, such as Reference Concentrations (RfCs). Ranges included floor, midpoint and ceiling.
- Range for EPA's TCE RfC was judged to be ***3 to 20 µg/m³***.
  - The results of the NTP study-based RfC were used to determine the floor and midpoint of this uncertainty range.
  - The highly controversial results from the Johnson et al. (2003) study-based RfC, while associated with low confidence, were nevertheless used to determine the ceiling level of this uncertainty range.
  - This 3 µg/m³ to 20 µg/m³ range was entirely within the wider individual uncertainty range from the Keil et al. (2009) study; therefore, this latter study was considered to be confirmatory.

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Need for Further Effort

- Continue this dialogue regarding vapor intrusion risk assessment issues, including agencies and responsible parties.
- Peer review proposed method for the noncancer risk range.
- Resolve discrepancies in TCE fetal heart findings from one lab compared with negative findings in all other labs.
- Determine appropriate TCE safe range & averaging time.

The Alliance for Risk Assessment (ARA) is a collaboration of 501c3 organizations. All contributions are tax-deductible. (https://www.givedirect.org/give/givefrm.asp?CID=4930)

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Collaboration thru *ARA* brings:

ARA – Building a Risk Assessment Community

Extra Slides

Imprecision Versus Uncertainty

- Imprecision of a RfC is on both sides of the RfC. This is because a 2nd expert group might estimate a RfC higher or lower than the 1st group, if given the same information.
- Uncertainty in a RfC, in contrast, lies mainly above the RfC. This is because RfCs are based on lower bounds on points of departure & uncertainty factors are known to be protective.
- For risk management decisions, uncertainty in the RfC is generally more important than imprecision. Managers are interested in making decisions that protect public health and uncertainties in a RfC are generally more informative.

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Developing the Range (con't)

- NAS (2009) suggested development of methods for noncancer toxicity that can determining hazard ranges.
- *ARA* project entitled "Beyond Science and Decisions: From Problem Formulation to Dose Response" responded to this NAS suggestion with 6 methods.
- We focus on 2 methods for the purposes of this work, specifically:
  - Use of biomarkers in the benchmark dose method; and
  - Estimate Risk Above the RfD Using Uncertainty Factor Distributions

For more information go to:

http://www.allianceforrisk.org/Projects/TCE.html

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