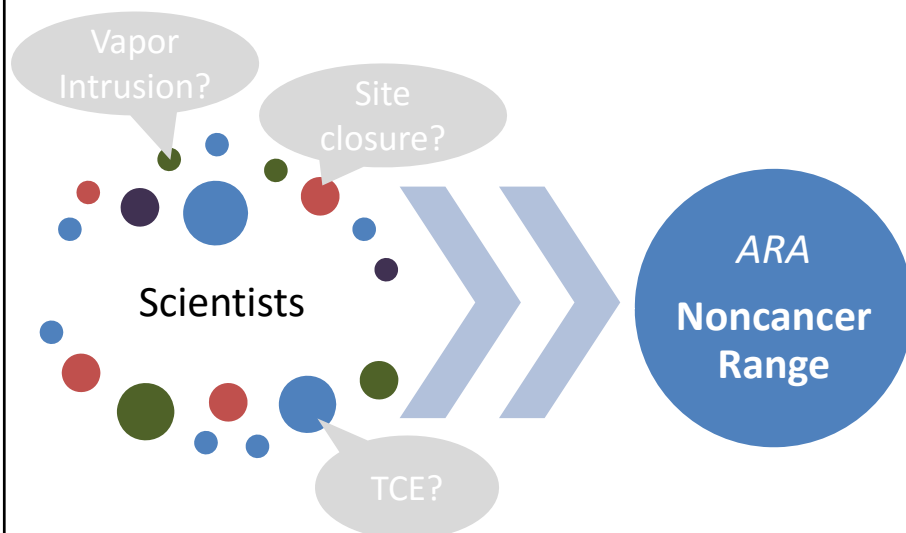


## Alliance for Risk Assessment (ARA)



### 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.

## 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  $\mu\text{g}/\text{m}^3$** .
  - 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  $\mu\text{g}/\text{m}^3$  to 20  $\mu\text{g}/\text{m}^3$  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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## 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  $\mu\text{g}/\text{kg}/\text{day}$ . 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)

- NAS (2009) suggested development of methods for noncancer toxicity that can determine 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

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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  $2 \mu\text{g}/\text{m}^3$  based on decreased thymus weight in female mice (Keil *et al.*, 2009);
  - RfC of  $2 \mu\text{g}/\text{m}^3$  based on fetal heart malformations in rats (Johnson *et al.*, 2003); and
  - RfC of  $3 \mu\text{g}/\text{m}^3$ , 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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## Imprecision Versus Uncertainty

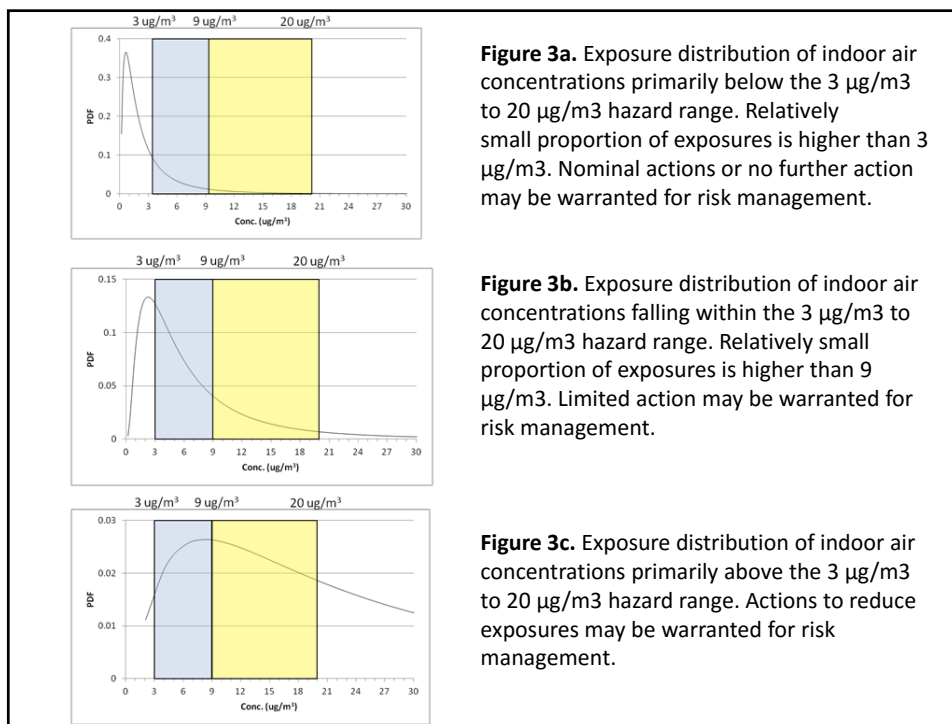
- Imprecision of a RfC is on both sides of the RfC. This is because a 2<sup>nd</sup> expert group might estimate a RfC higher or lower than the 1<sup>st</sup> group, if given the same information.
- Uncertainty in a RfC, in contrast, lies mainly above the RfC. This is because RfCs are based on lower 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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## Different Uncertainty Ranges for TCE RfCs

Table 7. Different uncertainty ranges for different TCE RfCs. All values are in  $\mu\text{g}/\text{m}^3$ . Shaded areas indicate best **overall uncertainty range** for risk management purposes.

Study	IRIS UF <sup>a</sup>	Steep <sup>b</sup> Slope	Confidence		Uncertainty Ranges		
			Critical <sup>c</sup> Effect	Point of <sup>d</sup> 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



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