Practical Guidance on the Development of a Non-cancer Hazard Range for Effective Risk Assessment and Risk Management of Contaminated Sites: A Case Study with Trichloroethylene and Other Chemicals

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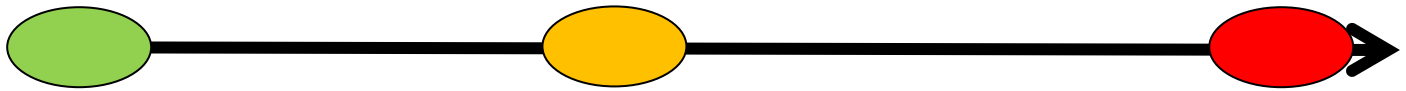
Problem Formulation

- Hazardous waste site remedial objectives for chronic exposure levels
- Communicating risk of exposure above RfC
- Prompt/short term exposure action levels
  - Prompt action exposure concentrations
    - EPA RAL (Could dose-response be considered?)
  - Application of chronic RfC to acute and subchronic exposures
  - Sampling to determine exposure concentrations for acute or subchronic effects
- Confounding effects of common indoor air background (TCE, Petroleum, PCE)

Common Past Risk Assessor Approach Remedial Objectives

- Cancer risk rules
  - Cancer Screening, Remedial Objectives and Health Effects Level are all established using a risk range of 10^{-6} to 10^{-4}



10^{-6} Screening Departure

Remedial Objective

10^{-4} Health Effects (commonly)

Purpose of 10^{-4} to 10^{-6} Cancer Risk Range

- Provides risk managers flexibility
  - Screening level and closure (RSLTs)
  - Majority are small sites not Superfund
- Balance acceptable exposure levels with property transaction needs:
  - Technical feasibility
  - Implementability
  - Timeliness
  - Economic considerations
  - Cultural of other concerns
- If balance is needed, how is NC risk assessment applied?

Historical Risk Assessor Non-Cancer Understanding

- Given:

- $RfC = \frac{NOAEL}{UF\ x\ MF}$

- NOAEL implies that any exposure level above this value will result in an adverse effect
- Strict Yes/No threshold overly simplistic understanding
- Allowed to exist because no real past impact
- Explore these issues with consideration of the "real" process.

Risk Assessor Attempts to Understand Process

- Risk Assessor Evaluating Process:
  - Is the NC RfC development method really a process for a threshold phenomenon?
    - Sub-threshold phenomenon for adverse effect in sensitive populations
  - Is there evidence that some bounding or hazard range is an accurate representation of this sub-threshold phenomenon?

Regulatory Risk Assessor Non-cancer Initial Understanding

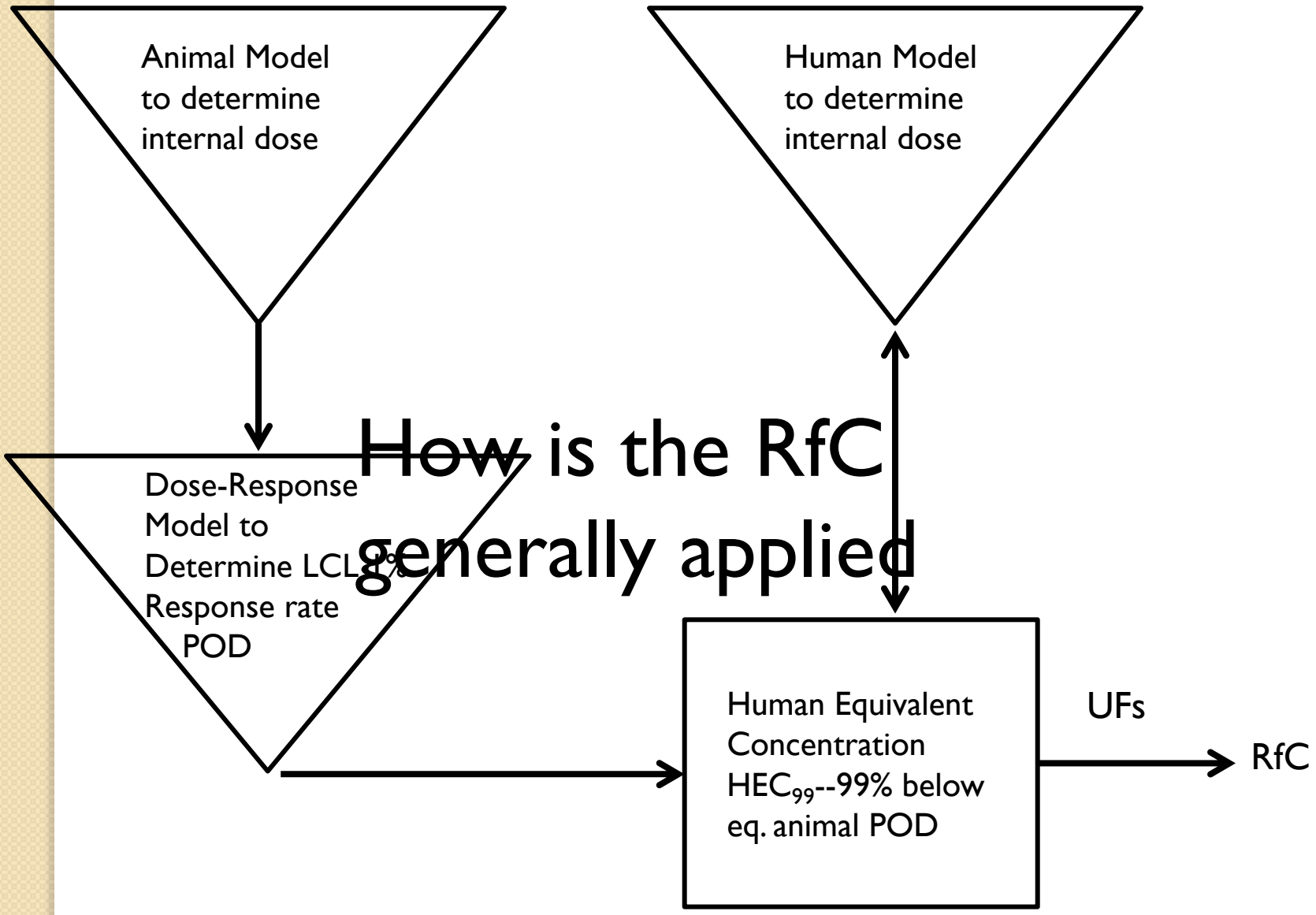
- IRIS RfC Definition-what does "with uncertainty spanning perhaps an order of magnitude" mean in the real world?
- Dourson et al 1996 defined,
  - ½ order magnitude either side (0.3 RfC-3RfC)
  - Above RfC (RfC-10RfC),
  - Below RfC (0.1RfC-RfC)
  - Above and Below (0.1RfC-RfC-10RfC)

Addressing Understanding

- What should be considered to understand "with uncertainty spanning perhaps an order of magnitude"
  - Uncertainty Factors (Margin of Safety)
    - Response to uncertainty generally provides a margin of safety
  - NOAEL to LOAEL
  - Slope of the BMD curve

Consider the Common Current RfC Development Process

- Can we still consider NC regulation and risk to be a strict yes/no threshold phenomena given:
  - Animal and human PBPK modeling,
  - BMD dose response curves,
  - Selection of a probability based POD (e.g. $BMDL_{01}$)
  - Additional Uncertainty Factors (3 & 3)



TCE RfC Determination Process

Regulatory Risk Assessor Misunderstanding

- How does precision of the RfC or the HQ screening level equation fit into the real world?

- $$IASL = \frac{THQ\ x\ AT}{(EF\ x\ ED\ x\ ET\ x \frac{1}{RfC})}$$

- HQ above 1 up to 2 has little meaning, cannot distinguish
  - (TCE = 2-4 ug/m^3)
- How does this impact the RAL at 3 x HQ

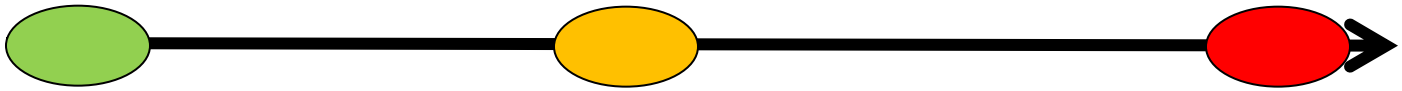
Regulatory Risk Assessor Confusion

- Develop a Chronic RfC
- Support the chronic RfC with a developmental study
- Then use the developmental supporting study as a standalone developmental RfC_{dt}
  - Consider: Would it have been possible to use the Johnson et al study to develop a stand-alone RfC_{dt} ?
  - EPA developmental and RAGs guidance-NO.

Common Regulatory Risk Assessor Action

- Most conservative position possible
- No balancing
  - No consideration of health effects/economic impact balancing
- What is regulatory intent?
- What does the science tell us?

Using Well Established Science and Science Policy, is there a Non-Cancer Range that Solves these Problems?



Non Cancer Screening

Remedial Objectives Level

Health Effects Level

Mid-Point of NC range may help guide risk based choices

Solves

- Risk Manager does have some flexibility to make risk based decisions (range)
- Communicate meaning of exposures above the RfC/RfD (range placement)
- Guidance on prompt action, immediate concern levels (ceiling)

Broader Application

- Is there a need for a broader context for the non-cancer hazard range application apart from TCE
- PCE
- As
- Cr 6+

Present a method to determine a range and the science and science policy that supports a range.