Risk Assessment: OEHHA and the VOC Exemption Process

Assessing and Managing Toxic Risk from Alternative VOC Compounds

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OEHHA's Role in the VOC Exemption Process

- **Substitution of a candidate compound for more reactive compounds could result in a significant increase in emissions of that compound.**
- **ARB staff, in conjunction with Office of Environmental Health Hazard Assessment (OEHHA) staff, generally conduct an environmental impact evaluation of the candidate compound.**
- **OEHHA reviews the potential health effects of "VOC exempt" compounds under our general mandate to provide support to ARB and the Air Districts on health issues from air pollutant exposures.**

Hazard Identification and Risk Characterization

- **Hazard identification and risk characterization procedure sources:**
- **2008 "Air Toxics Hot Spots Program Technical Support Document for the Derivation of Noncancer Reference Exposure Levels"**
- **2009 "Air Toxics Hot Spots Program Technical Support Document for Cancer Potencies"**

Risk Characterization Values

- **Interim Reference Exposure Levels (RELs) and Cancer Potency Factors (CPFs) are developed using methodologies contained in the documents mentioned using existing toxicity data for the candidate chemical.**
- **Unlike Hot Spots RELs and CPFs, the interim RELs and CPFs do not receive peer review by ARB's Scientific Review Panel.**

Hazard Identification

- Chemicals may have multiple effects, including:
  - Acute and/or chronic organ/system toxicity
  - Developmental/reproductive toxicity
  - Carcinogenicity
- Conduct literature search for:
  - Human epidemiological or controlled exposure studies
  - Animal toxicity studies

Risk Characterization: Noncancer Dose-Response Assessment

- **Characterization of the relationship between the dose of a chemical and the incidence of an adverse health effect in the study or experimental population.**
- **For noncarcinogens this process results in an acute or chronic REL.**
- **A REL is meant to be a "safe" exposure level at or below which no adverse noncancer health effects are anticipated.**

Dose-Response Assessment: Point of Departure

- **Point of Departure (POD): the starting point in terms of either an exposure (e.g., mg/m^3 of air, mg/L of water) or a dose (e.g., mg/kg-day) from a study to extrapolate to a REL.**
- **PODs:**
  - **NOAEL: no observed adverse effect level**
  - **LOAEL: lowest observed adverse effect level**
  - **BMD: Benchmark Dose**
- **BMD: Modeled dose or exposure associated with a specified rate of response in a study**
  - **BMD approach is preferred to use of NOAELs/LOAELs**

REL Calculation

1. **Identify POD (a dose or a concentration)**
2. **Multiply by appropriate time adjustments (e.g. intermittent exposure to continuous exposure, Haber's Law)**
3. **Multiply by appropriate dosimetric adjustment (e.g. Human Equivalent Concentration)**
4. **Divide the value by appropriate uncertainty factors (UFs).**

$$\text{REL} = \frac{\text{POD} * \text{adjustments}}{\text{UFs}}$$

Uncertainty Factors

- Used to address datagaps when extrapolating from study results to the human population.
- May range from 1 to 10, maximum total UF is usually 3000.
- Interspecies uncertainty factor (UF_A)
  - To extrapolate from animals to humans
- Intraspecies uncertainty factor (UF_H)
  - To extrapolate from healthy average humans to sensitive humans

Uncertainty Factors

- **Subchronic uncertainty factor (UF_S)**
  - **To extrapolate from subchronic study to chronic exposure**
- **LOAEL to NOAEL UF**
- **Data deficiency factor (UF_D)**
  - **Usually employed if developmental, reproductive studies have not been conducted, or when database is poor**

Cancer Dose-Response Assessment: Data Types/Modeling

- **Human epidemiological cancer data**
  - **linear dose-response model (regression analysis usually applied).**
- **Animal tumor data**
  - **Biologically based models: Linearized multistage model.**
  - **Empirical models: Benchmark dose method (a mathematical function providing best fit to the observed dose-response data). Linear extrapolation rather than UFs applied to POD.**
  - **Benchmark dose method preferred.**
  - **Assume potency scales between species as ¾ power of body weight.**

Cancer Risk Characterization

- **Endpoint is quantal (you either have it or you don't).**
- **Dose response assessment determines a carcinogen's potency - expressed as lifetime risk per unit dose.**
  - **Cancer potency (slope) factor: $mg/kg\text{-}day^{-1}$**
  - **Unit risk: $(\mu g/m^3)^{-1}$**
- **Dose response is generally linear at low dose – no threshold. There is some increment in risk even at very low exposures.**
- **We use cancer potency factors to estimate cancer risk**

Cancer Risk = Exposure X Potency

Cancer Risk Characterization

- **Risk values are upper bound estimates for an exposed population.**
- **Estimates are believed to be health conservative.**
- **Do not predict risk for a specified individual.**
- **Risk estimates for multiple carcinogenic exposures usually considered additive.**
- **Procedures address risk for whole life or at least 1 or more years.**