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Health-Based OELs

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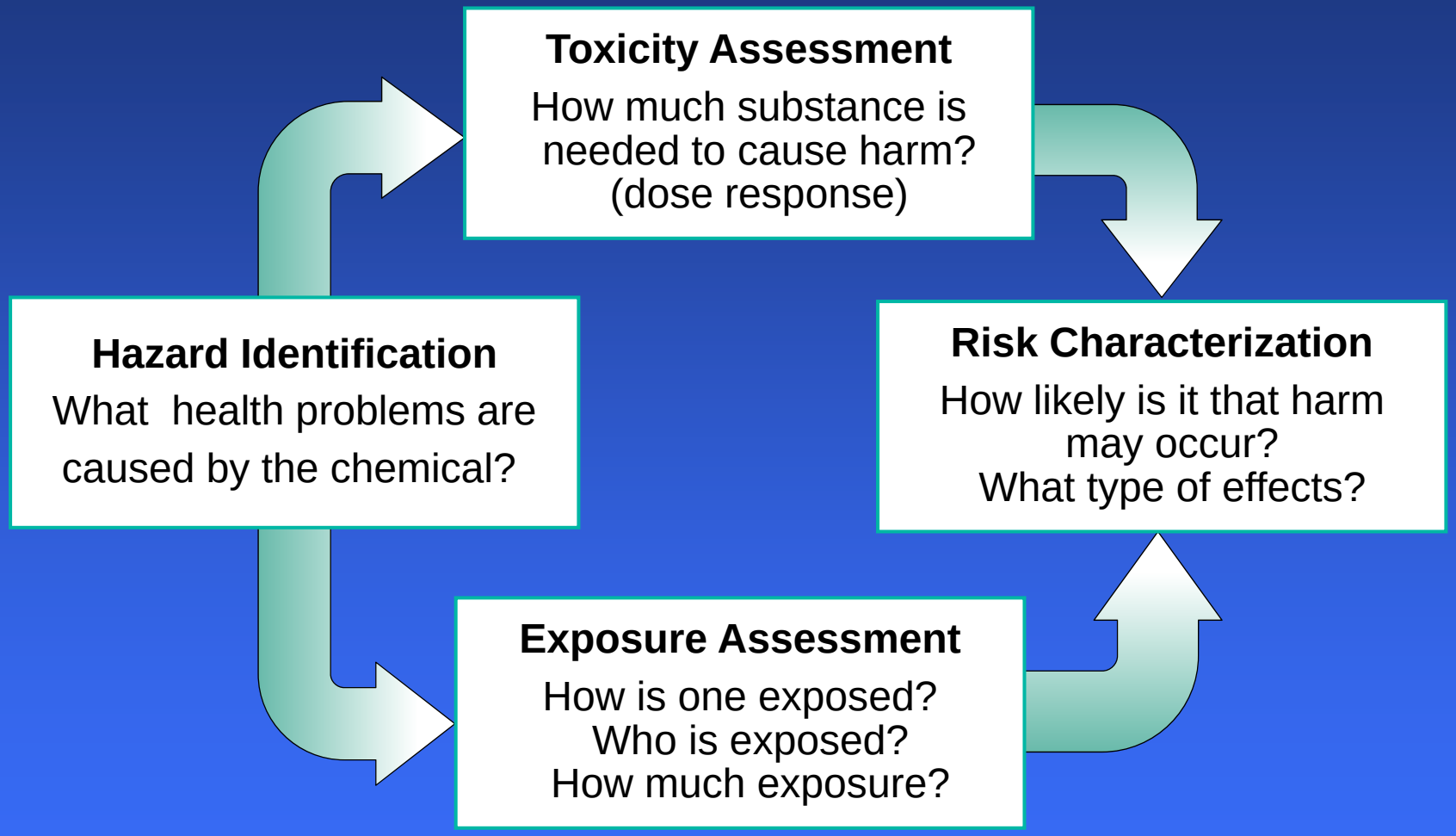
Health Risk Assessment –How Scientific is it?



The 4 Steps of Risk Assessment

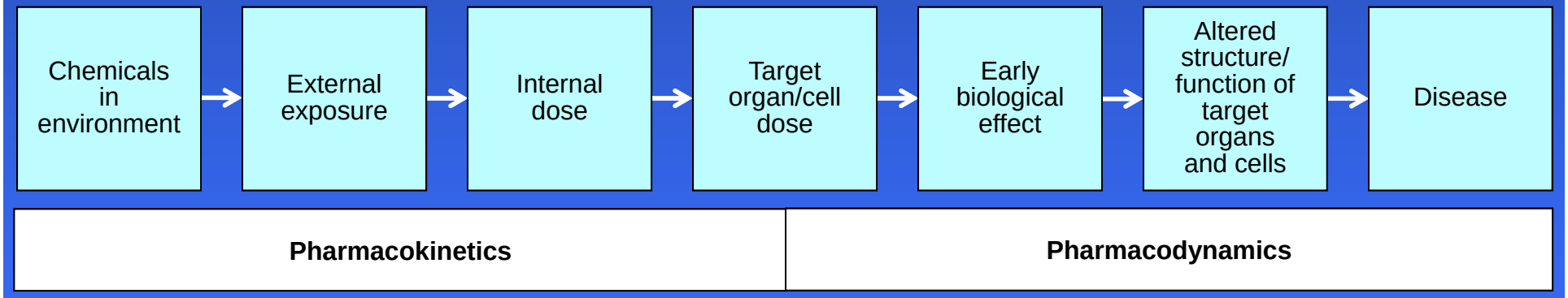
Step 1: Hazard Identification

Step 1: Hazard Identification:

- **Can exposure cause increased incidence of health effects?**
  - Epidemiological studies
  - Animal studies
- **Focus on "Weight of Evidence" approach**

Hazard Identification: From Exposure to Disease

Advances in epidemiology and toxicology are bringing greater knowledge about each step of the process and even about the fine molecular details within each step



The 4 Steps of Risk Assessment

Step 2: Dose Response Assessment

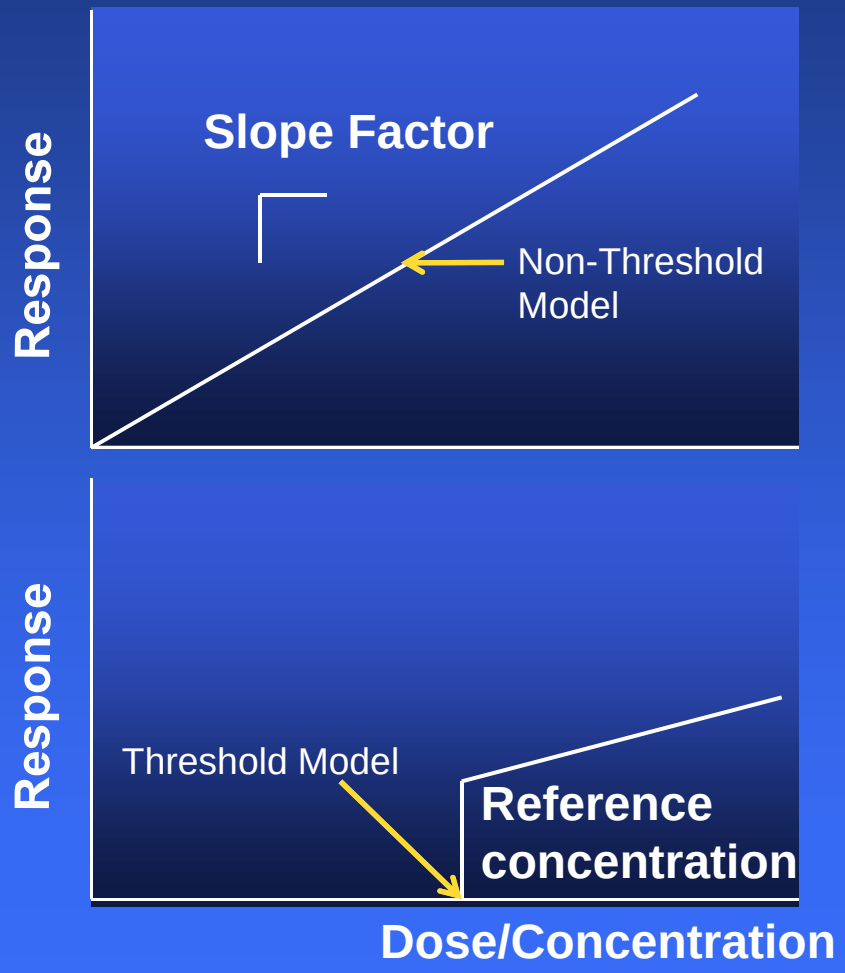
Basis of Toxicity Criteria

- **Epidemiologic data**
  - Workplace studies
  - Population studies
  - Poisonings
  - Human endpoint known – dose?
- **Studies in animals**
  - High to low dose extrapolation
  - Dose known – human endpoint ?

Dose Response Assessment Models

Carcinogens

Non-Carcinogens



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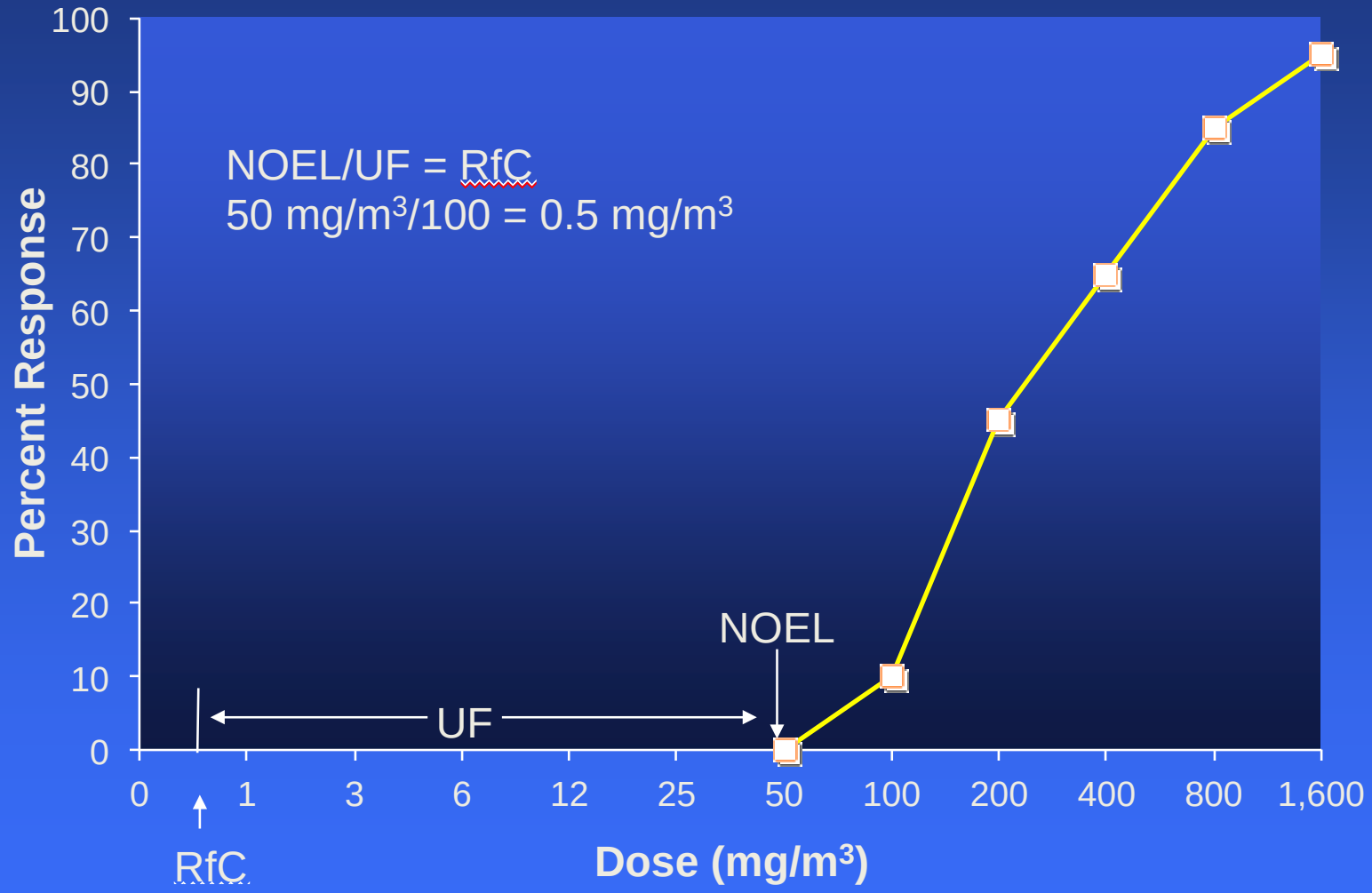
Non-Cancer Effects – NOEL approach

- **Employs no observable effect level (NOELs) or lowest observable effect levels (LOELs)**
- **Employs uncertainty factors (UFs: 10–10,000)**
- **NOEL/UF = RfC (acceptable daily concentration)**
- **"reference concentration" (RfC) Assumes some dose below which adverse effects are not anticipated**
  - Includes "sensitive" subpopulations

Reference Concentration



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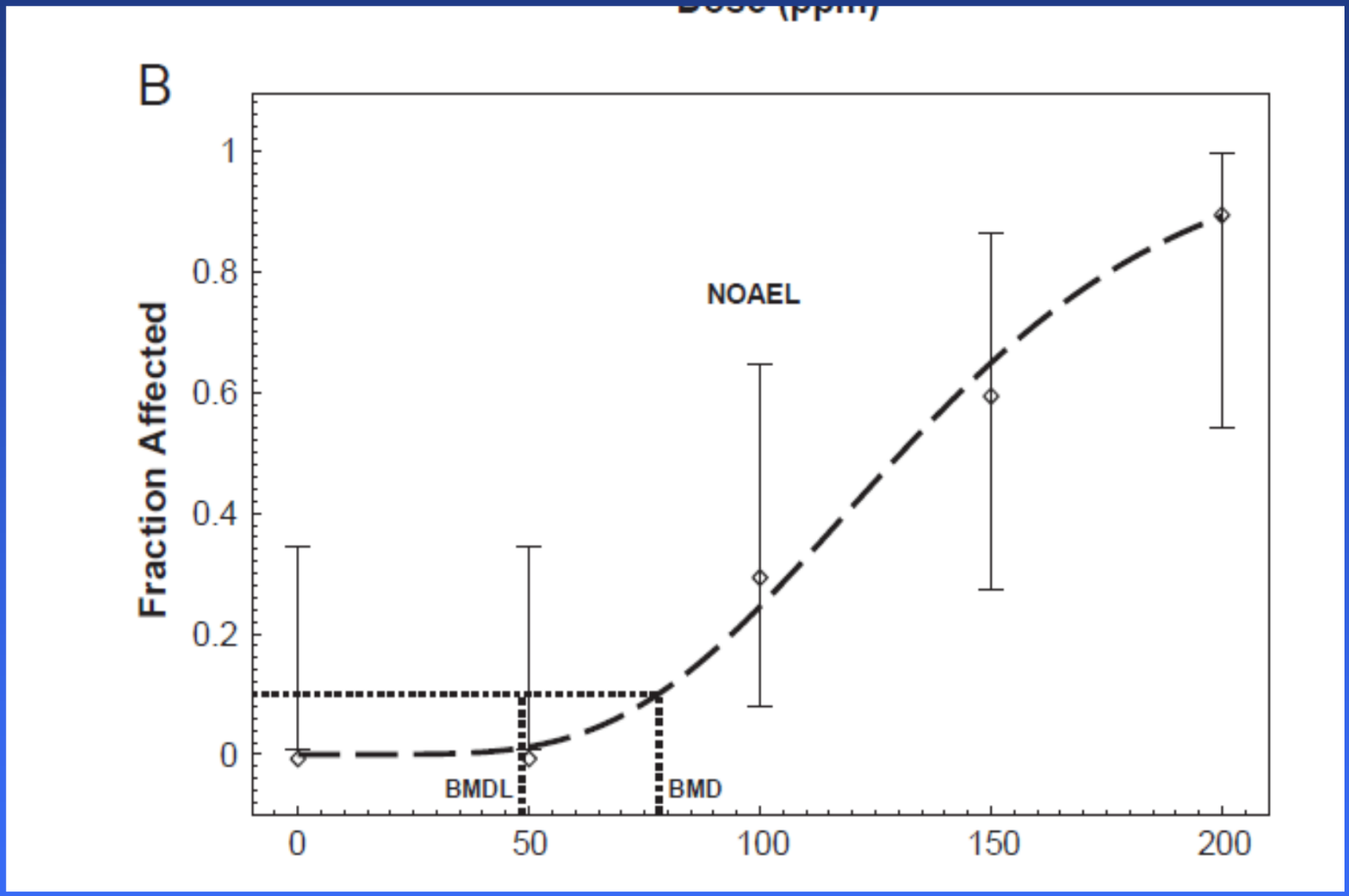
Non-Cancer Effects – Benchmark Dose (BMD) modeling

- **Mathematical models used to estimate the dose that produces a predetermined change in the response rate of an adverse effect – Point of departure (POD)**
  - dose that causes a low but measurable target organ effect (e.g. a 10% increase in number of rats with fatty liver).
- **Can estimate the threshold dose when no NOEL can be established**
- **Uncertainty calculated as confidence interval**

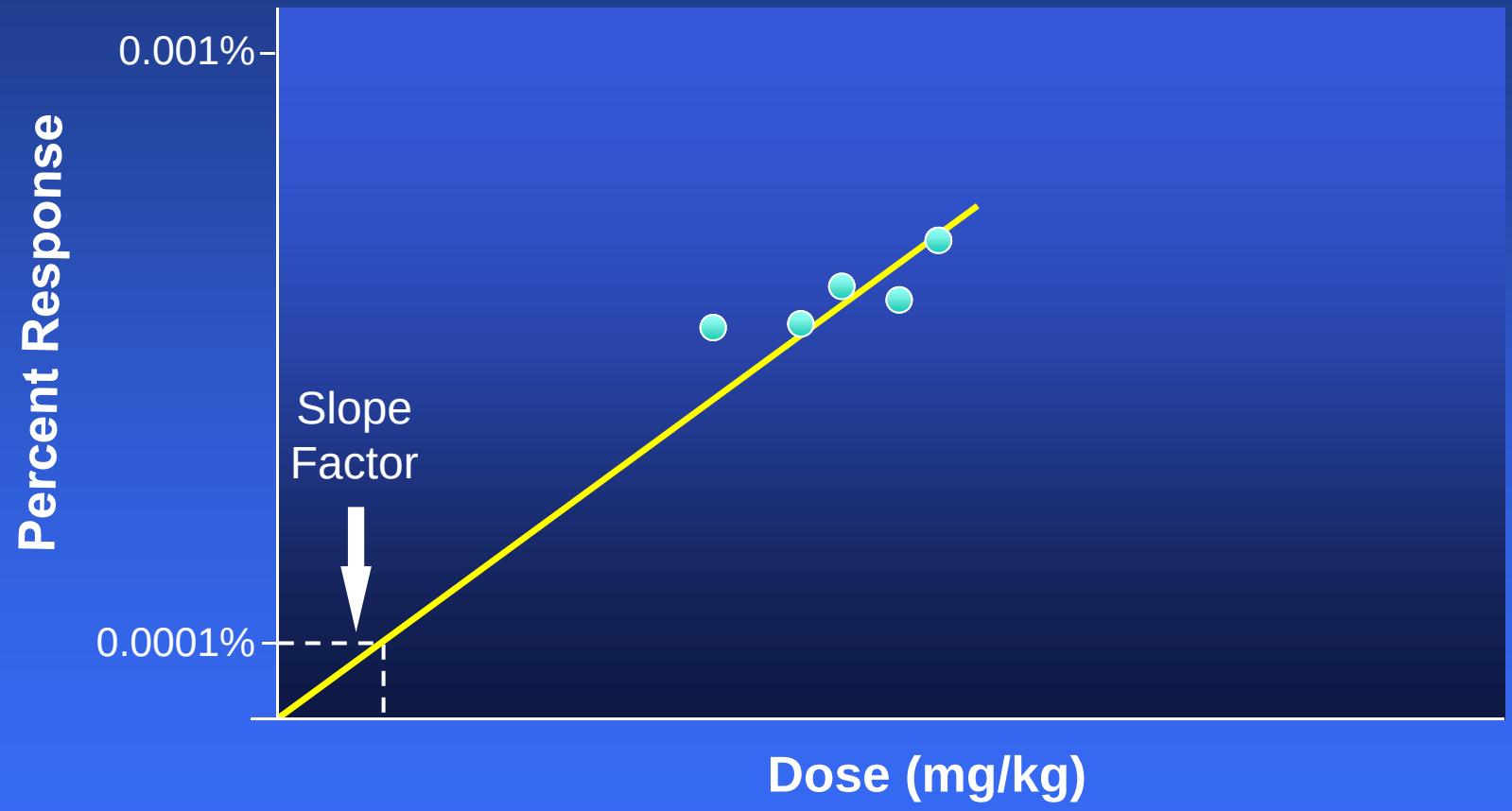
Non-Cancer Effects- Benchmark Dose



Cancer Slope Factors (Unit risk factors)

- **Unit risk factor (URF) mathematical risk of cancer from a unit air concentration**
- **Slope Factor (oral) mathematical risk of cancer from a unit oral dose**
- **Usually modeled from high dose animal studies**
- **Mathematical dose extrapolation models**
  - When mode of action at tumor site not known, or mutagenic agent – default linear extrapolation

Cancer Slope Factors



Inhalation Unit Risk

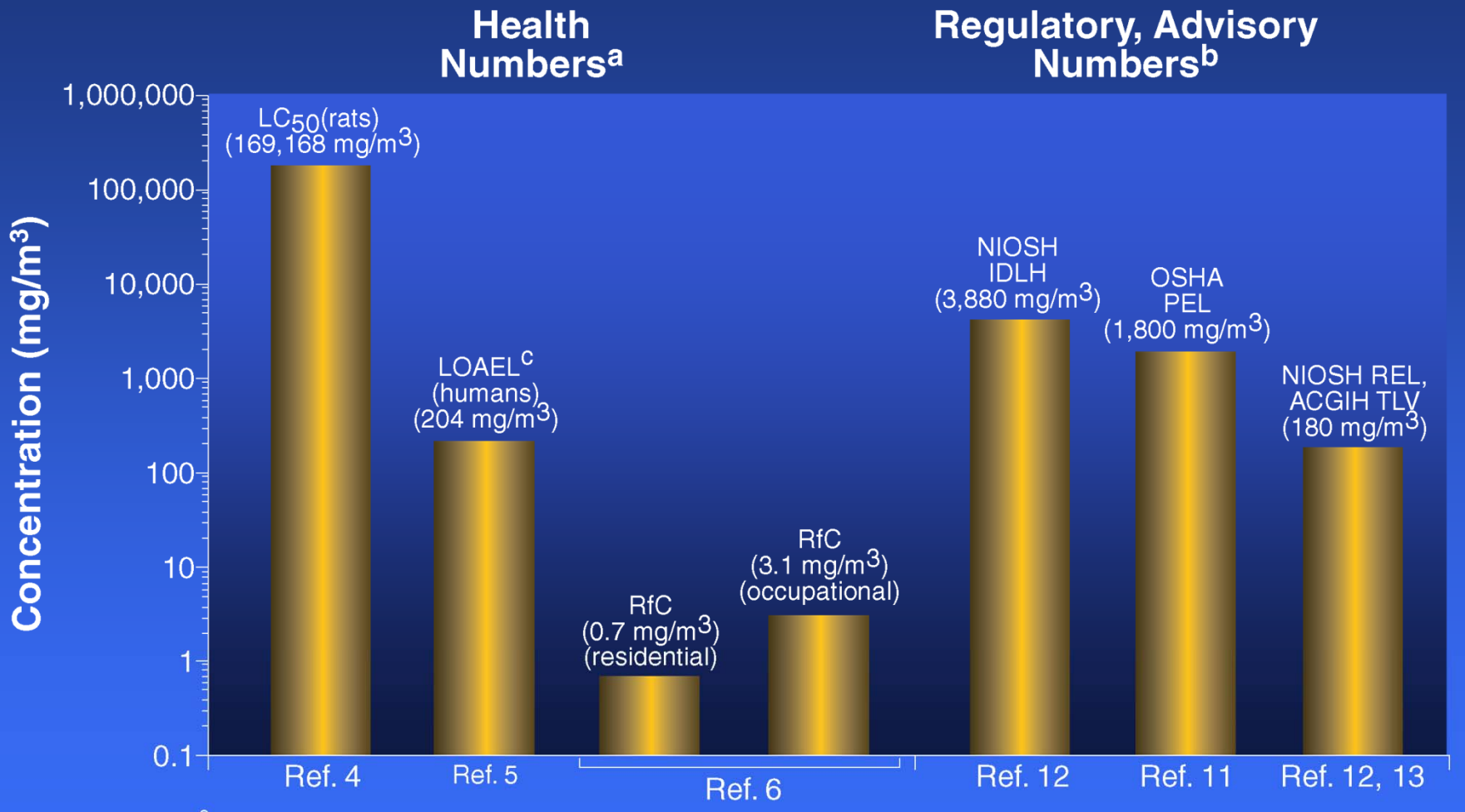
- The upper-bound excess lifetime cancer risk estimated that results from continuous exposure to an agent at a concentration of 1 µg/m³ in air.

- If unit risk = 2×10^{-6} per µg/m³, 2 excess cancer cases per 1,000,000 people (upper bound estimate) are expected to develop... if exposed daily for a lifetime to 1 µg of the chemical per m³ of air.

Dose Response: Numerical Toxicity Values

- **Cancer**
  - Cancer slope factor (CSF): Oral and dermal $(mg/kg\text{-}day)^{-1}$
  - Unit risk factor (URF): Inhalation $(ug/m^3)^{-1}$
- **Non-cancer**
  - Reference dose (RfD): Oral and dermal mg/kg-day
  - Reference concentration (RfC): Inhalation $\mu g/m^3$

Inhalation Exposure to Hexane—Non Carcinogen



[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory.
[c] The LOAEL is from the critical study used as the basis for the former EPA RfC of 0.2 mg/m³.
Source: http://www.epa.gov/ttn/atw/hlthef/hexane.html

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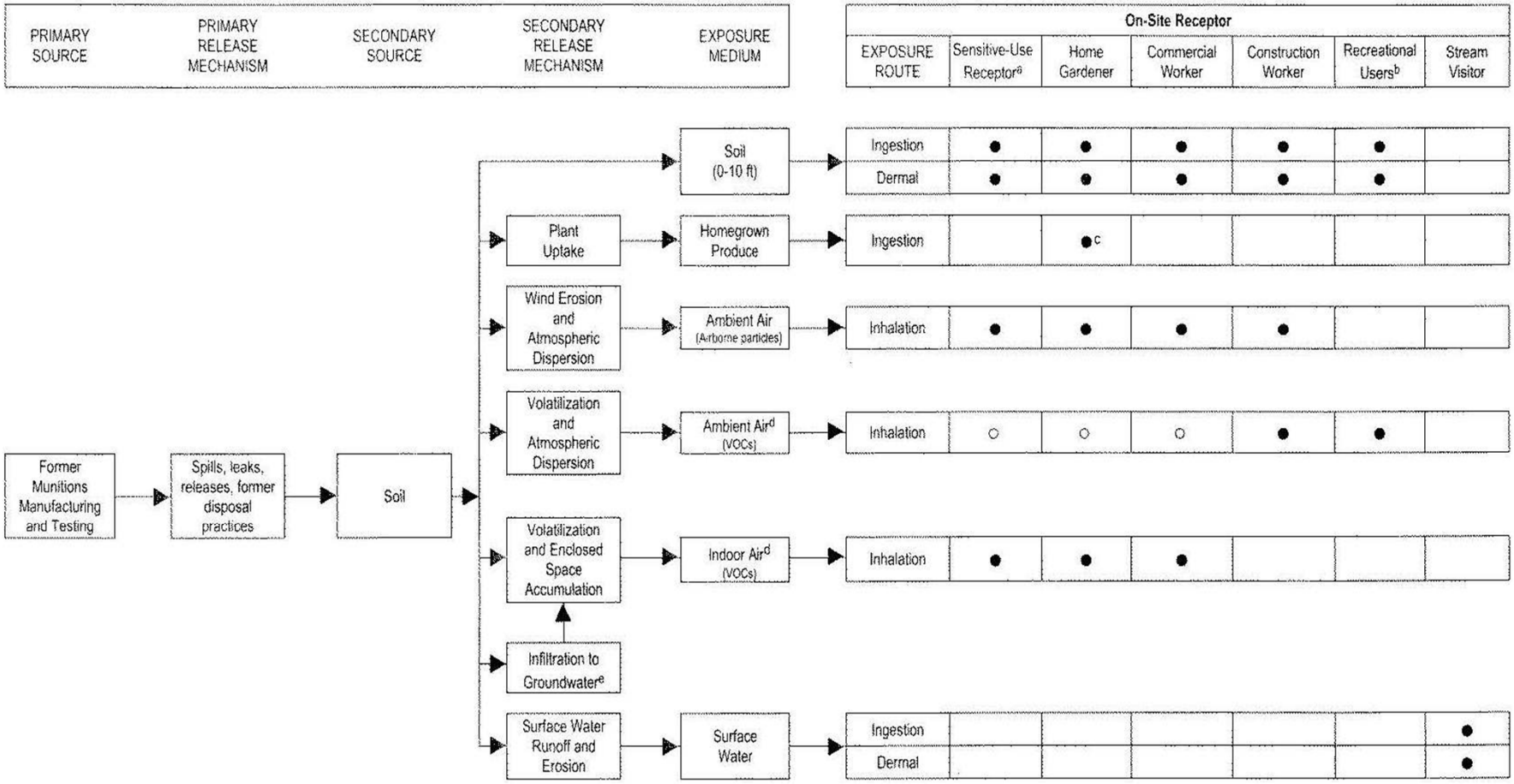
The 4 Steps of Risk Assessment

Step 3: Exposure Assessment

Exposure Conceptual Site Model



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Worker Exposure Assessment

- Body weight: 70 kg
- Exposure Frequency: 250/365 days
- Exposure Duration: 25 working years /70 year lifetime
- Breathing rate: 20 m^3/day
- Exposure time: 8 – 10 hour days

Basic Inhalation Exposure Equation

$$EC = \frac{C \times ET \times EF \times ED}{AT}$$

Where:

EC = Exposure Concentration (mg/m^3)

C = Concentration in Air (mg/m^3)

ET = Exposure Time (hrs/day)

EF = Exposure Frequency (days/year)

ED = Exposure Duration (years)

AT = Averaging Time (days) * differs for carcinogens vs. non-carcinogens

The 4 Steps of Risk Assessment

Step 4: Risk Characterization

Step 4: Inhalation Risk Characterization

Carcinogenic effects:

$$\text{Risk} = \text{EC}\ (\text{mg/m}^3) \times \text{URF}(\text{mg/m}^3)^{-1}$$

Noncarcinogenic effects:

$$\text{Hazard Quotient} = \frac{\text{EC}\ (\text{mg/m}^3)}{\text{RfC}\ (\text{mg/m}^3)}$$

Risk is a probability (i.e., 1 in a million) of the chemical to cause cancer after a lifetime of exposure
EC = Exposure Concentration
URF = Unit Risk Factor

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Use equations to back calculate an acceptable air concentration

$$EC = \frac{C \times ET \times EF \times ED}{AT}$$

Where:

EC = Exposure Concentration (mg/m^3)

C = Concentration in Air (mg/m^3)

ET = Exposure Time (hrs/day)

EF = Exposure Frequency (days/year)

ED = Exposure Duration (years)

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EPA Caveat

"These values are upper bound estimates of excess cancer risk potentially arising from lifetime exposure to the chemical in question. A number of assumptions have been made in the derivation of these values, many of which are likely to overestimate exposure and toxicity. The actual incidence of cancer is likely to be lower than these estimates and may be zero."

Region IX EPA, 1989

"The results of the baseline evaluation should not be taken as a characterization of absolute risk."

RAGS-A p.8-25

OEL versus EPA TCE Assessment

	Hazard Identification	Dose Response	Exposure Assessment	Risk Characterization
TLV	Weakly mutagenic CNS effects > 100 ppm Cohort study: no increase in cancer incidence Case control study: high concentrations increased renal cancer	TLV basis: CNS, Cognitive decrements Renal toxicity	na	A TLV-TWA of 10 ppm (54 mg/m^3) should protect against the CNS effects of TCE as well as the potential other effects including rental toxicity
EPA	Decreased thymus weight Increased fetal cardiac malformations* Kidney tumors	Non cancer: $HEC_{99,\ BMDL01}$ 10 fold UF RfC = 2 µg/m^3 Cancer: URF = (4.0 x 10^{-6} µg/m^3)$^{-1}$	8/24 hrs 250/365 days 25/70 years	3 µg/m^3 (cancer) 8 µg/m^3 (non-cancer) 24 µg/m^3 (non-cancer urgent response)

* 30 – week drinking water study – route to route extrapolation using PBPK model

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Risk-based versus OELs for common VOCs

	OSHA PEL ($\mu g/m^3$)	ACGIH TLV ($\mu g/m^3$)	Risk Based Commercial Indoor Air Concentration ($\mu g/m^3$)
Benzene	3,195 (1 ppm)	1,597 (0.5 ppm)	0.14 (0.04 ppb)
PCE	678,323 (100 ppm)	169,580 (25 ppm)	0.693 (0.10 ppb) 2 .0 (0.3 ppb)

Traditional OEL versus Environmental Risk Assessment Considerations

Environmental

- Sensitive populations
- Numerous chemicals
- Lack of chemical awareness
- No PPE available
- Lack of population studies – numerous confounding factors
- Lacks economic/practical consideration

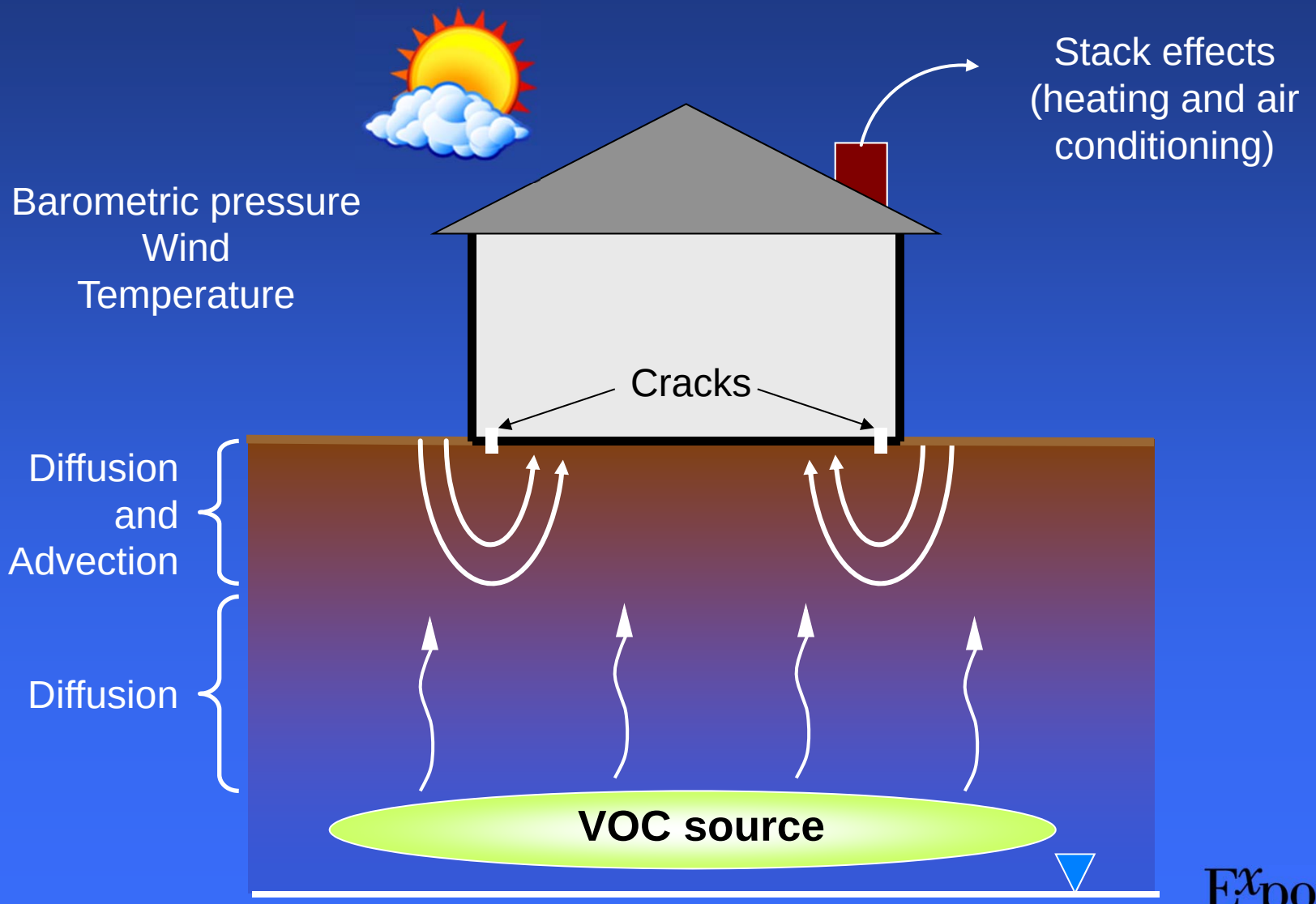
Worker

- Healthy Worker
- Fewer chemicals
- Training/Chemical awareness
- PPE available
- Population studies may be available - ground truth
- Practicality often considered

How are EPA risk-based evaluations relevant to you?

- **Exposure assessment and toxicity tools are used to develop risk based screening concentrations… for soil, groundwater, contact surfaces and …AIR**
  - Resultant air concentrations are MUCH lower than occupational exposure levels
  - For carcinogens – must select target acceptable risk level and then back- calculate acceptable air concentration
  - In some workplace settings the risk-based levels may take precedent over OELs

Example: Vapor Intrusion Conceptual Model



Permissible Exposure Levels (PELs): OSHA

- **PEL: Maximum concentration of a chemical in the air that a worker may be exposed to without respiratory protection (Cal. Code of Regs., tit. 8, § 5155)**
  - OSHA regulates workspaces and exposures to contaminants associated with job duties.
  - Address worker exposures to contaminants in workplace air from chemical handling or use, and **NOT** environmental air contaminants originating from the subsurface
  - **NOT** indices of toxicity and **NOT** intended to protect against "continuous, uninterrupted exposures or other extended work periods" and MAY not sufficiently protect office workers or other workers onsite
  - **NOT** appropriate criteria for evaluating vapor intrusion risk and should **NOT** be used as screening levels

Conclusions

- **Industrial hygienists should understand basic health risk assessment principles**
- **Risk assessment used to evaluate environmental media and establish acceptable levels**
  - Soil, water, AIR
- **Industrial hygienists well suited in fundamentals**
  - Toxicology, data analysis, exposure assessment and risk characterization

Conclusions

- **The lack of consistency in methods used to develop risk-based versus traditional occupational levels will likely receive more attention in future ...**
  - The future of OELs???