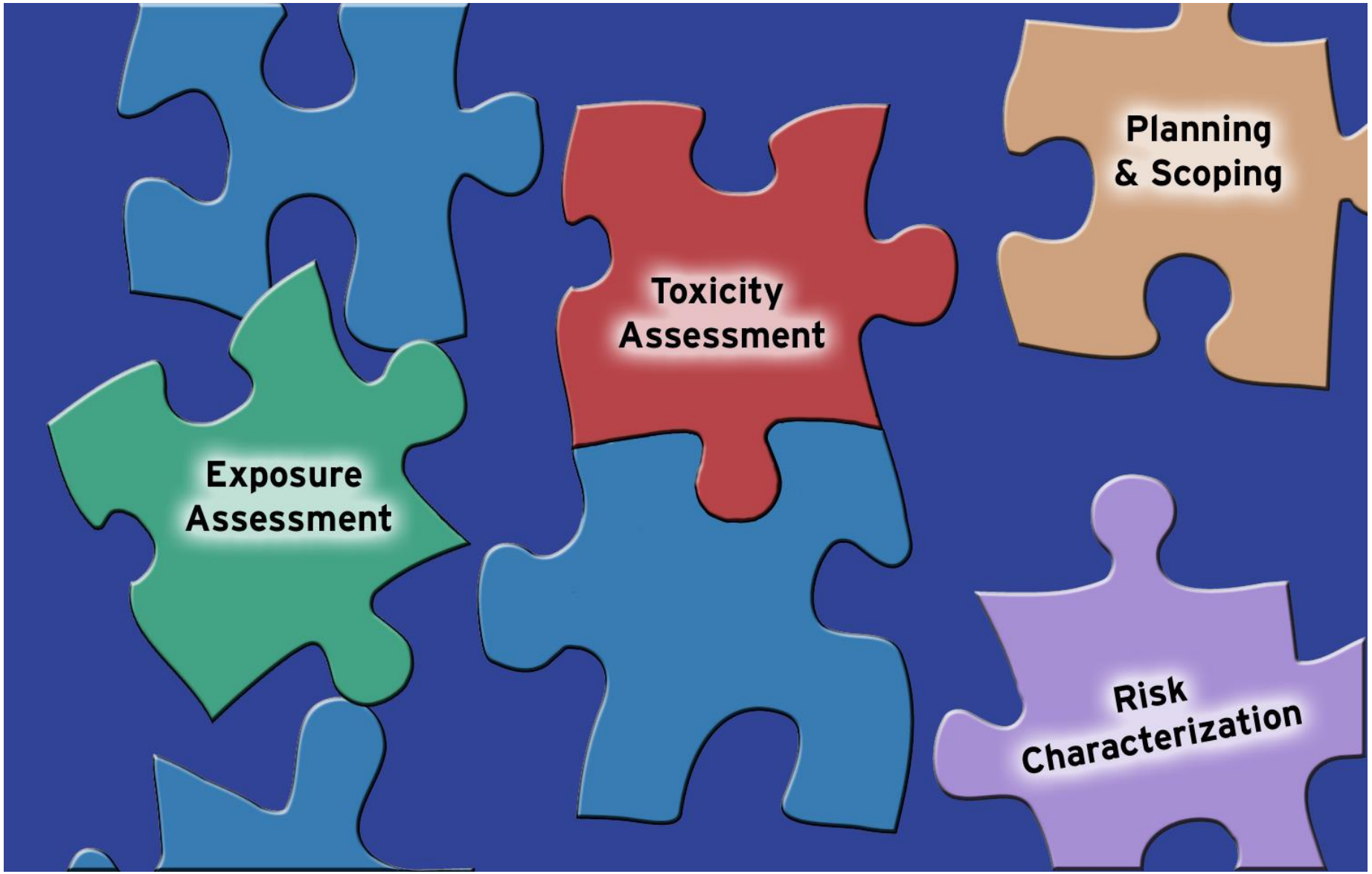
Fundamentals of Exposure Assessment and Calculating Risk Results



Learning Objectives

- **Know Terms and Concepts**

  Understand and use key concepts and terms related to air toxics Risk Assessment.

- **Identify Steps and Tools**

  Identify the basic steps and tools in conducting/evaluating Risk Assessments.

- **Optimize Learning**

  Boost learning results in the study of Risk Assessment and continue learning after instruction.

Learning Objectives

- **Estimate Risk**

  Able to generate simple risk estimates.

- **Access Resources**

  Recognize and access resources to aid in conducting/evaluating Risk Assessments.

- **Select/Interpret Data**

  Select data and appreciate that interpretation of data may be required to support each of the risk assessment components

- **Judge Data Quality**

  Judge the quality of data obtained and be able to decide on adequacy of data for intended purposes. Describe limitations of the selected data.

Learning Objectives

- **Interpret/Critique Results**

  Interpret and critique assessment results.

- **Understand the Information Needs of Decision Makers**

  Able to describe a basic process of risk-based decision making and the information needed.

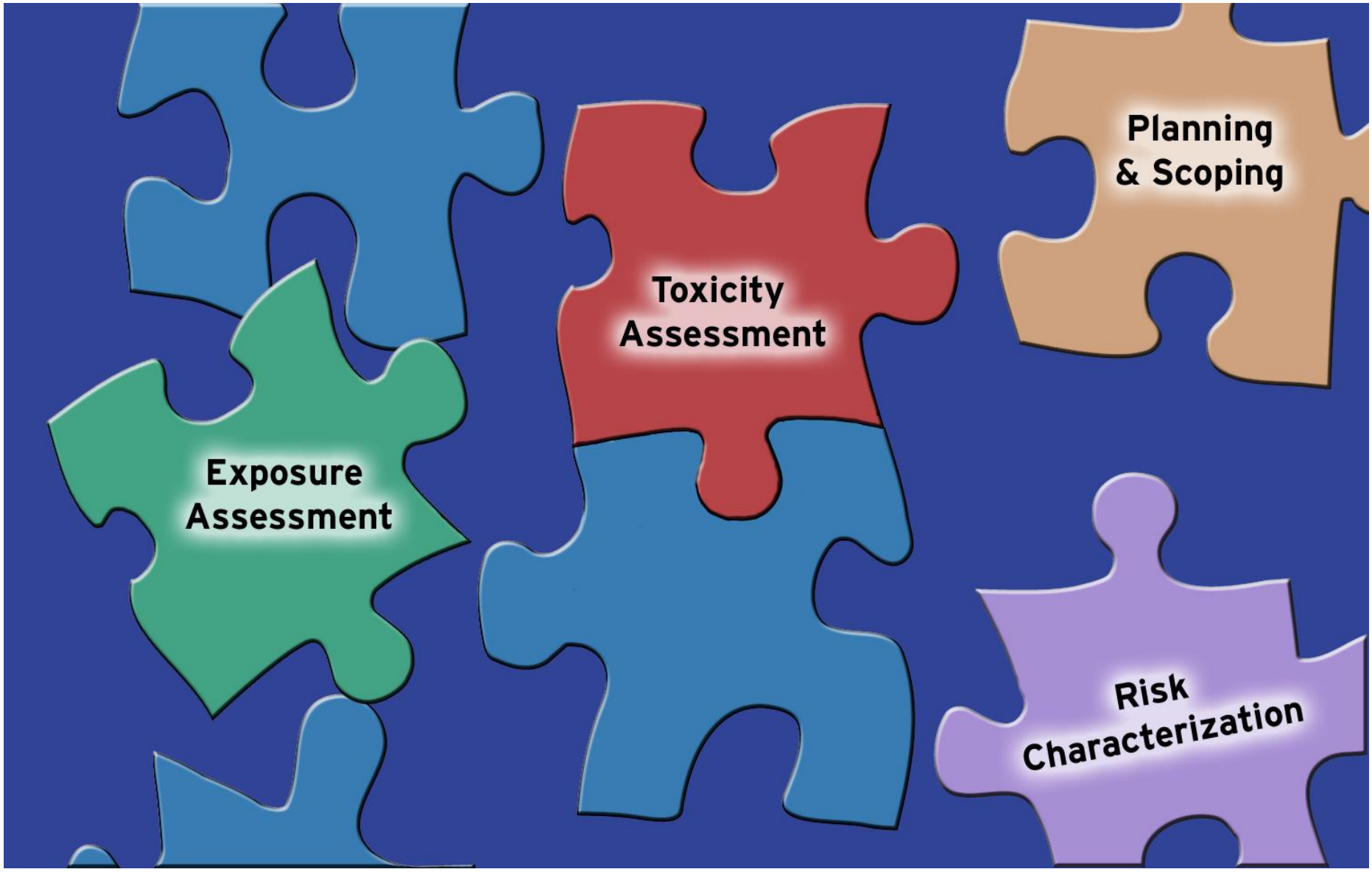
- **Understand the Purpose of Planning and Scoping a Risk Assessment**

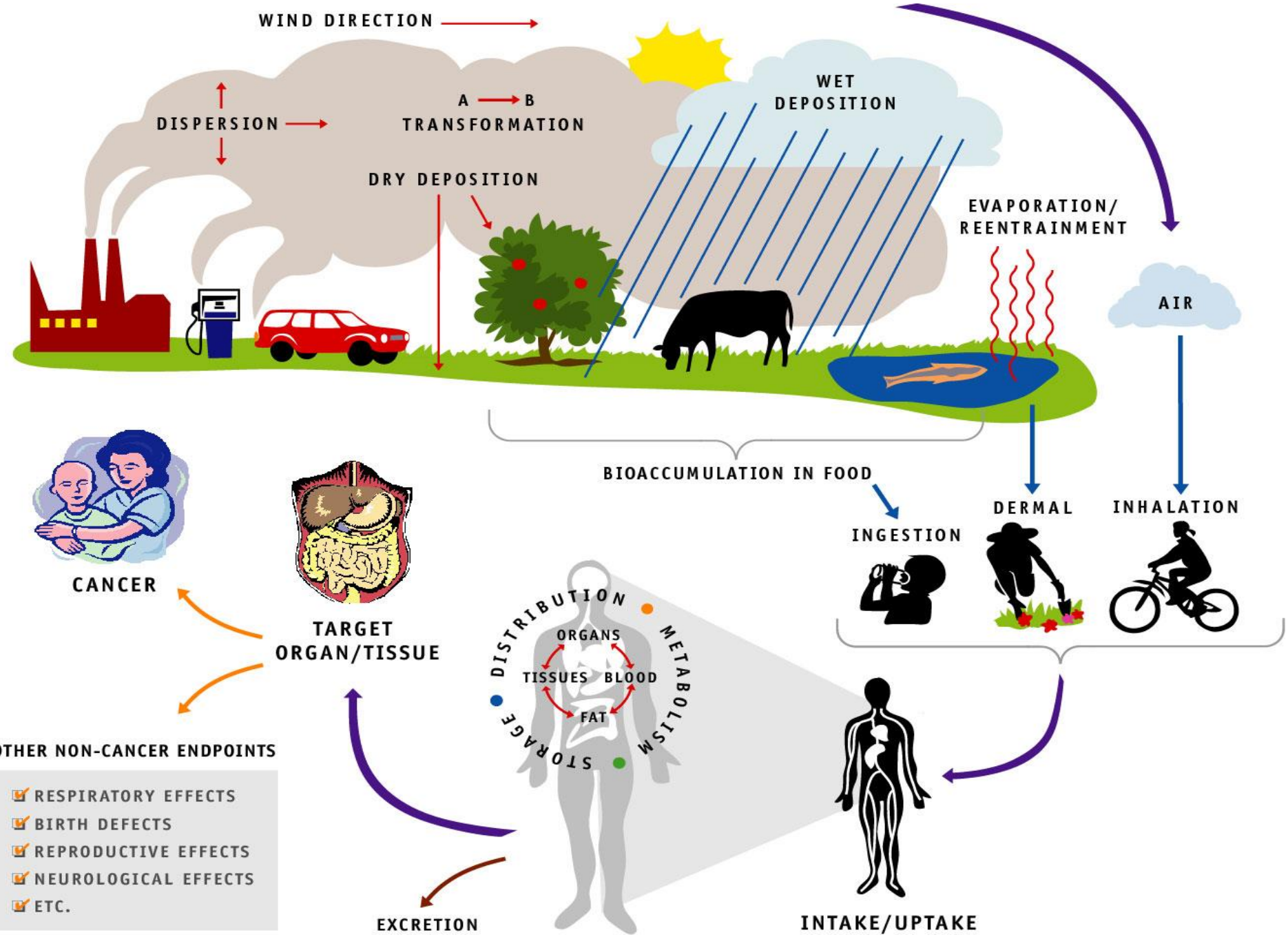
  Can describe the basic parameters and importance of scoping and planning. Able to describe the how the balance of rigor and uncertainty within time and resource constraints affects a Risk Assessment.

Agenda

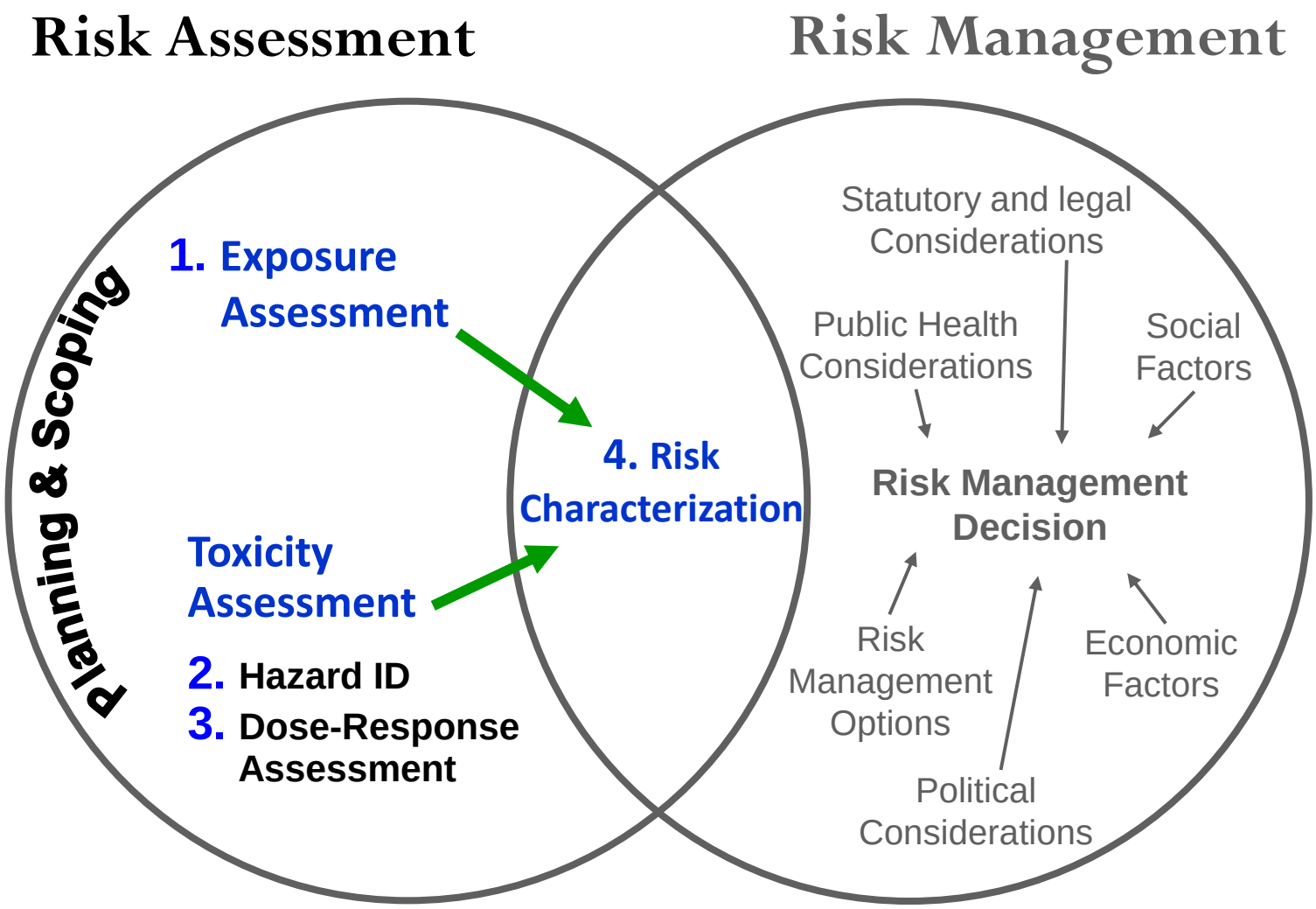
1:00-1:08	Introductions & Learning Objectives
1:08-1:20	Risk Assessment Overview
1:20-1:35	Community Case Study Background
1:35-2:25	Planning & Scoping
2:25-2:35	10 MINUTE BREAK
2:35-3:20	Exposure Assessment
3:20- 4:00	Toxicity Assessment
4:00-4:05	5 MINUTE BREAK
4:05-4:15	Risk Characterization
4:15-4:50	Discussion (35 min)
4:50-5:00	Q&A, Wrap-up

The Air Toxics Risk Assessment Process




WIND DIRECTION
DISPERSION
A → B
TRANSFORMATION
DRY DEPOSITION
WET
DEPOSITION
EVAPORATION/
REENTRAINMENT
AIR
BIOACCUMULATION IN FOOD
INGESTION
DERMAL
INHALATION
CANCER
TARGET
ORGAN/TISSUE
DISTRIBUTION
METABOLISM
STORAGE
ORGANS
TISSUES
BLOOD
FAT
OTHER NON-CANCER ENDPOINTS
RESPIRATORY EFFECTS
BIRTH DEFECTS
REPRODUCTIVE EFFECTS
NEUROLOGICAL EFFECTS
ETC.
EXCRETION
INTAKE/UPTAKE

General Four Step Risk Assessment Process



General Air Toxics Risk Assessment Process: Planning and Scoping

Exposure Assessment

Who is exposed?

What chemicals are they exposed to?

Toxicity Assessment

Is a chemical toxic?

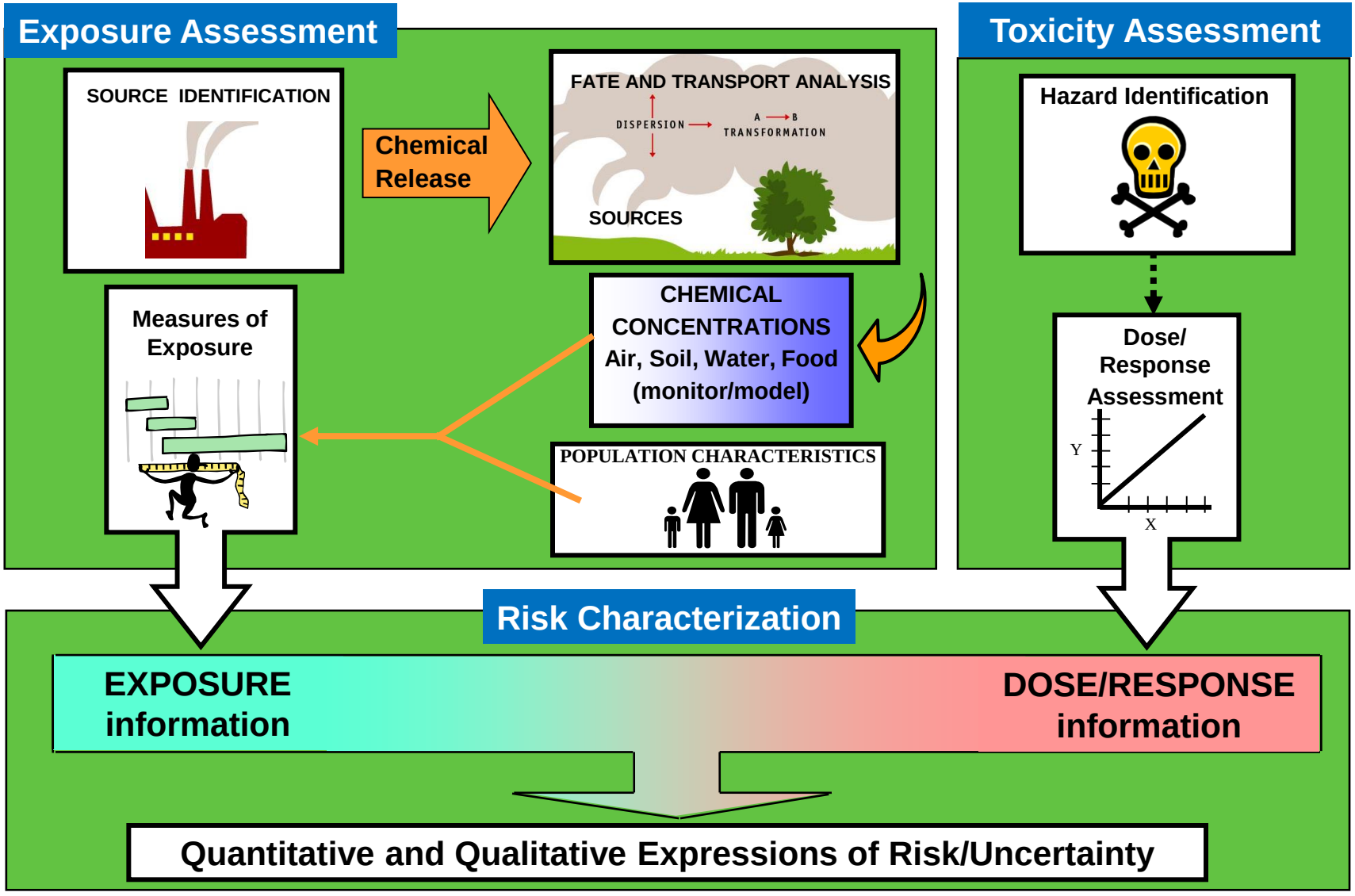
What is the relationship between the dose of a chemical and the response that results?

Risk Characterization

What is the likelihood the exposure will result in an adverse health effect?

How sure are we our answers are correct?

Detailed Air Toxics Risk Assessment Process: Planning and Scoping



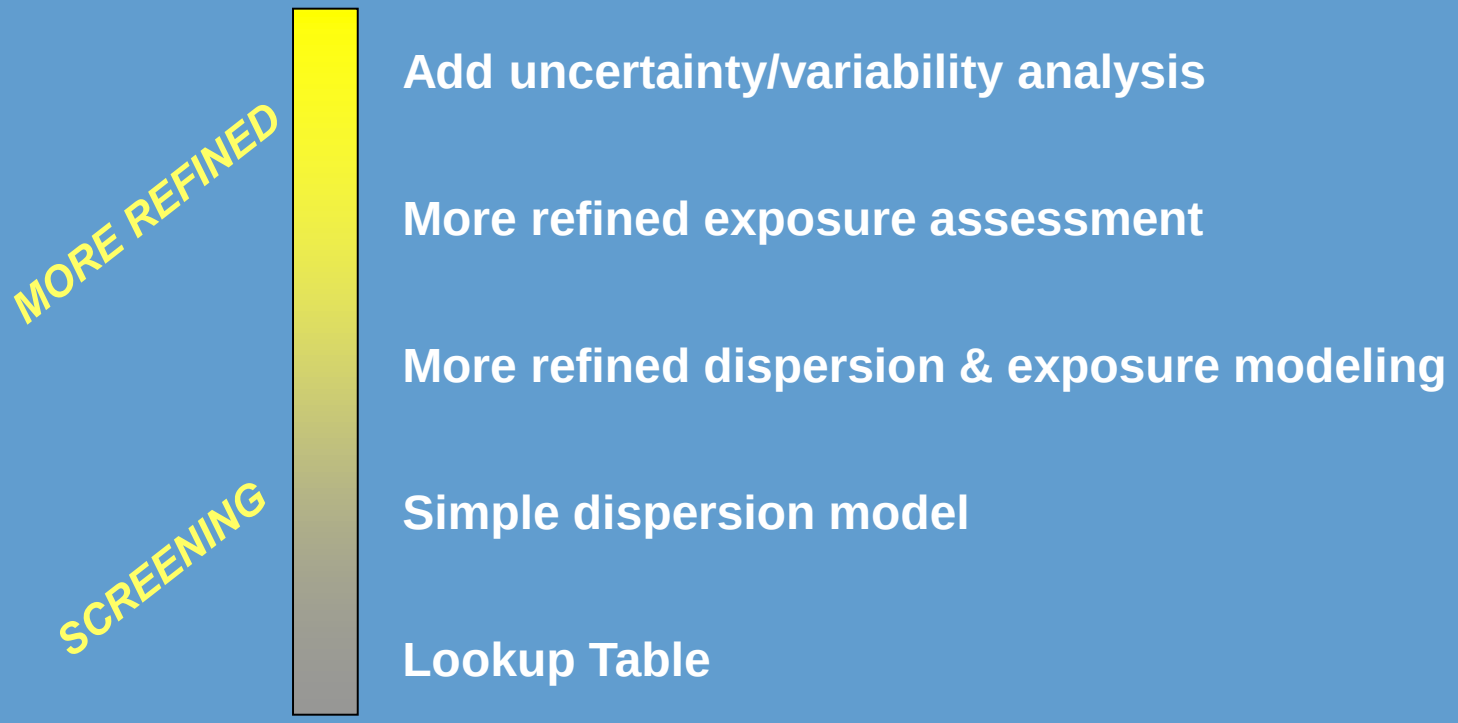
General Risk Assessment Process

Let's restate this 4-step risk assessment process with a simple mathematical formula:

$$\text{RISK} = f\,[(\text{Measure of Exposure}), (\text{Measure of Toxicity})]$$

Risk Assessment Continuum: Tiered Approaches to the Process

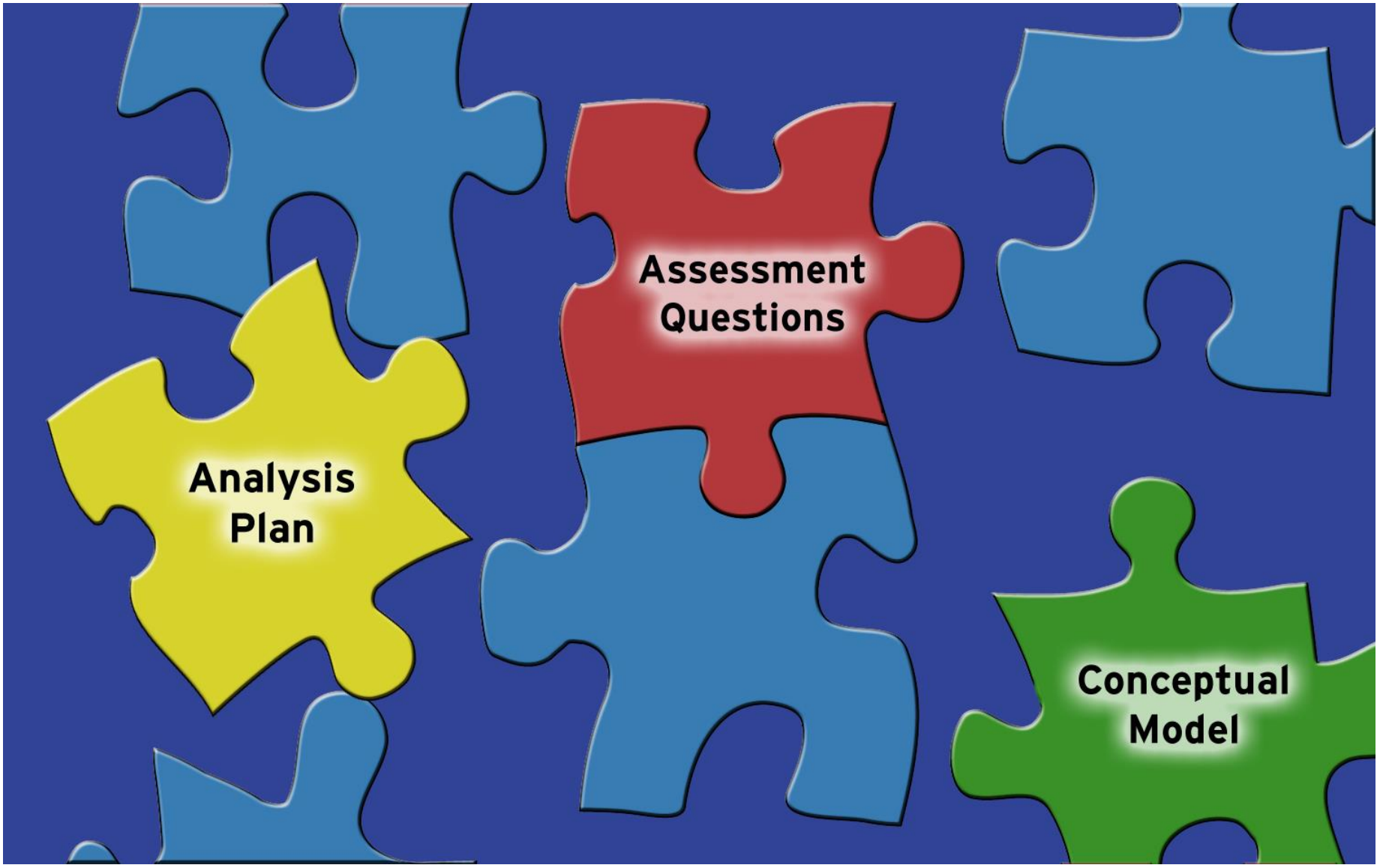
Complete study-specific data, no assumptions; higher cost, lower uncertainty



No data, all assumptions; lower cost, high uncertainty

Questions?

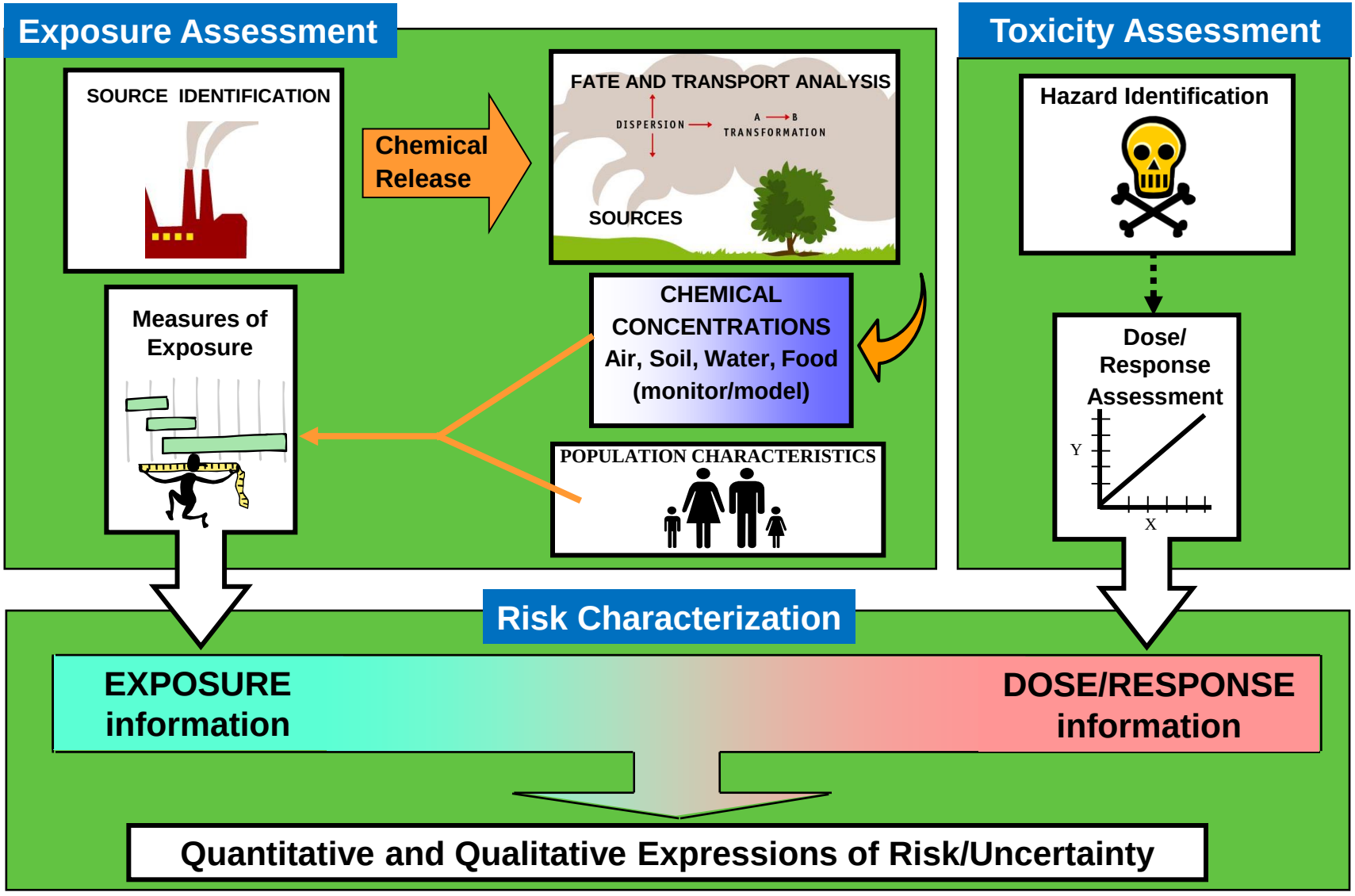
Planning & Scoping



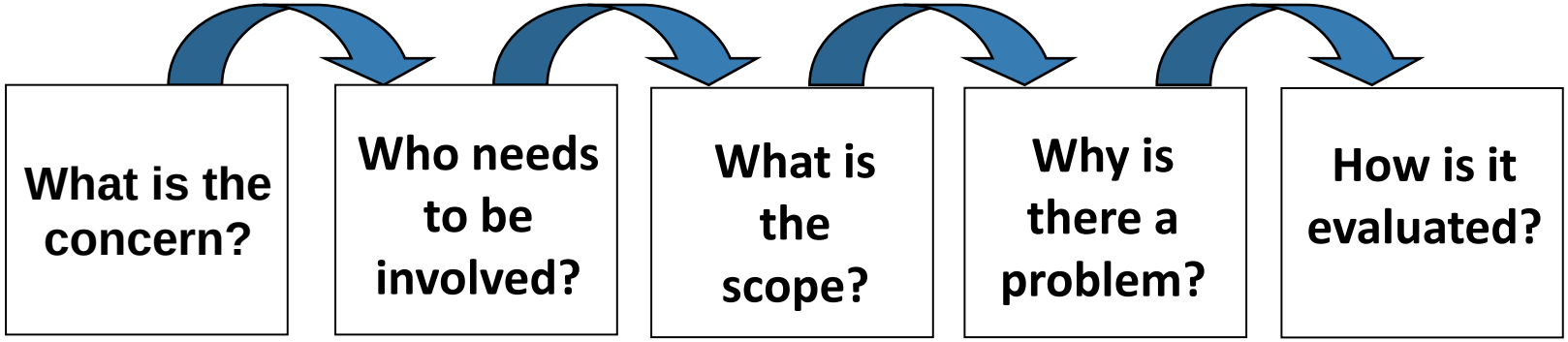
We'll cover these questions

- **What** is "planning and scoping"?
  - Also called "P&S"
- **Why** do it?
- **Who** is involved?
- **What** is the process?
- **What** products are produced?

Detailed Air Toxics Risk Assessment Process: Planning and Scoping



Detailed Air Toxics Risk Assessment Process: Planning and Scoping



P&S is the first step of the air toxics risk assessment process.
It is a deliberate and deliberative process that:

- Identifies the problems to be assessed
- Identifies participants in the process
- The bounds of the analysis (i.e., elements to be included/excluded from the analysis)
- A description of the interrelationship between stressors and receptors
- Articulates the overall analysis plan for the assessment

Why do P&S?

What are the benefits?

- To assure that analyses focus on problem(s) of concern to stakeholders
- To promote stakeholder “buy in” to assessment results
- To improve risk assessment “transparency”
- To help organize the assessment by providing a clear plan of analysis and process for documenting what was actually done
- Ensure that data of sufficient quantity and quality are developed to answer the questions the assessment has set out to answer

P&S team must understand

- The perceived problem
- The questions to be answered
- The scope and bounds of the study
- The quality and quantity of data necessary to answer assessment questions

P&S team must understand

- The methods by which data will be developed
- Roles and responsibilities of all players
- Available resources and schedules
- Documentation requirements & products required

What is the Scope?

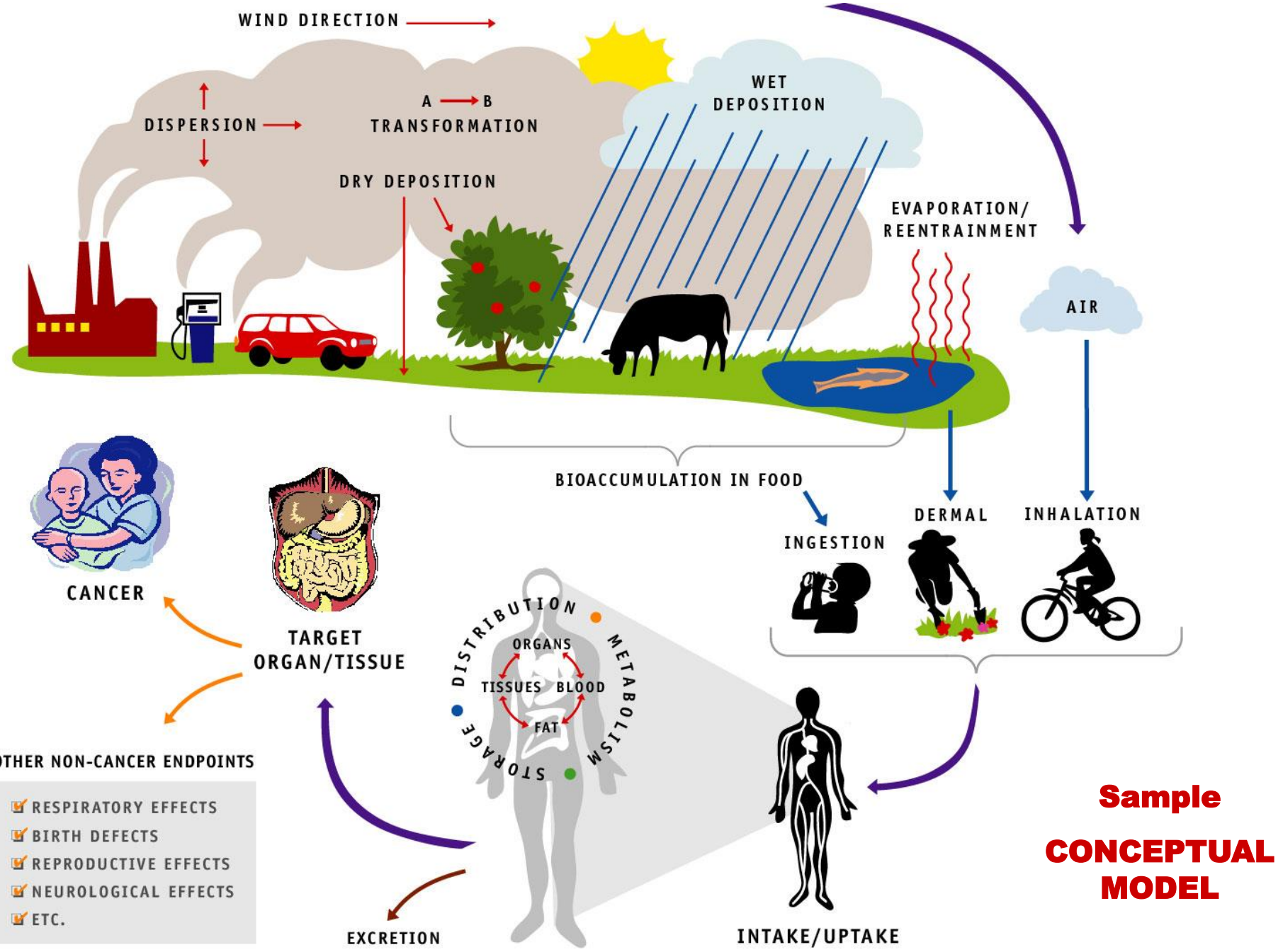
Define the scope by listing and answering critical assessment questions:

- What specific **sources** are to be included?
- What specific **chemicals of potential concern** (COPCs) are to be included?
- What are the specific **physical boundaries** of the study area?

What is the Scope?

Define the scope by listing and answering critical assessment questions:

- What potential **exposure pathways** are to be evaluated?
- What potentially **exposed populations** are to be assessed?
- What types of **health risks** are we interested in evaluating?
- What is our detailed **rationale** for all of the above?



Sample

CONCEPTUAL MODEL

How is it evaluated?

Critical elements of an analysis plan:

- **Sources of COPCs**
  - What is our plan to develop information on source identity/ location/characteristics?
- **Exposed populations and pathways**
  - How will we confirm/deny the presence of potentially exposed populations and potential exposure pathways?
- **Exposure concentrations of COPCs**
  - What methods will we use to measure and/or model COPCs in environmental media at the points of exposure?
- **Exposure conditions**
  - What methods will we use to evaluate how people contact contaminated media (e.g., activity patterns)?

How is it evaluated?

Critical elements of an analysis plan:

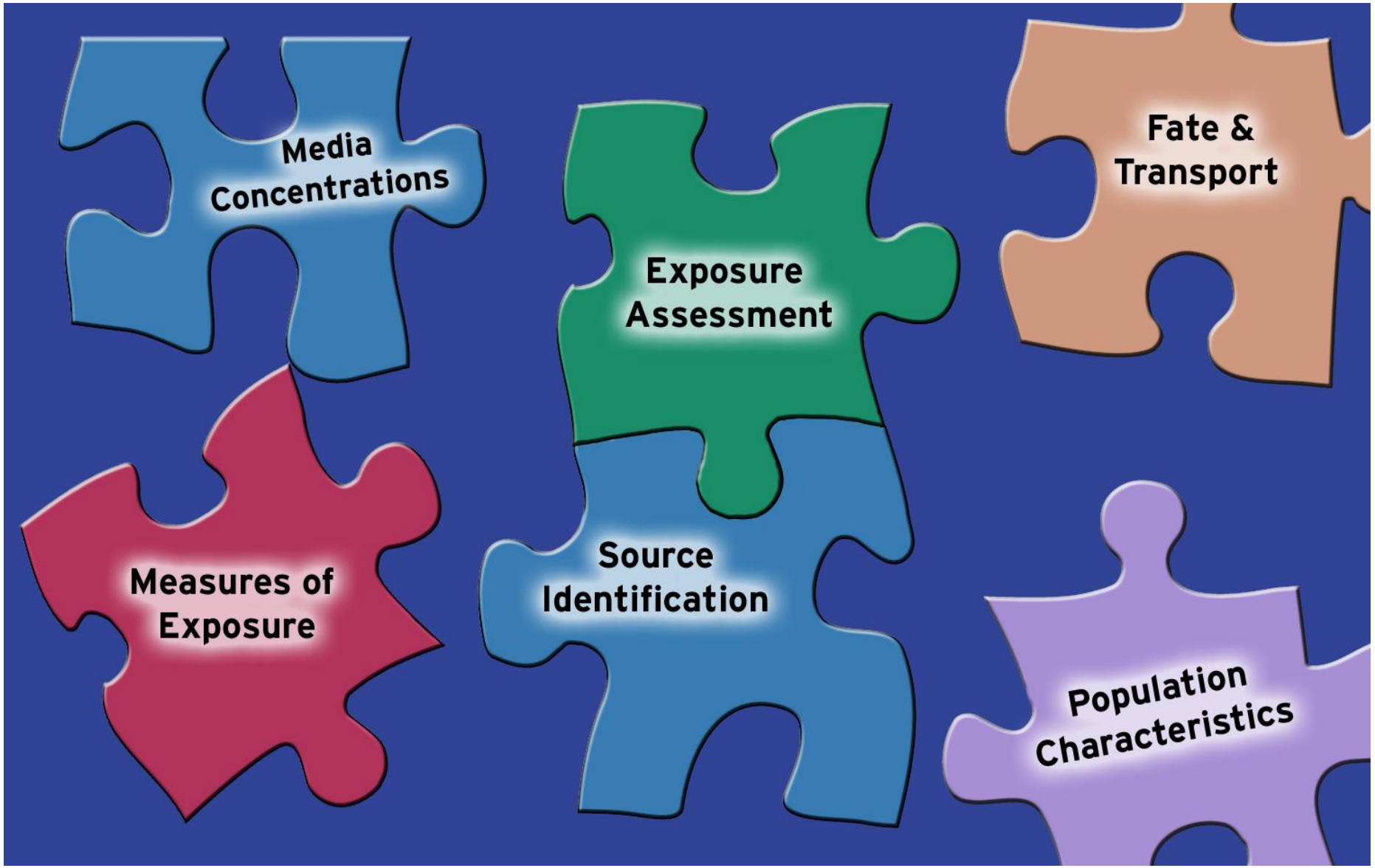
- **Toxicity Information for COPCs**
  - What data sources will we use?
- **Risk Characterization**
  - What methods will we use to characterize risk, evaluate uncertainty, and report the results?
- **QA/QC**
  - What are the requirements/processes for each step in the assessment?
- **Documentation**
  - What are the documentation requirements?
- **Players**
  - Who will perform the various activities?
- **Schedule**
  - What is the schedule for each step?

To Summarize

- Planning and scoping (P&S) is an **organizing** step that precedes the actual analysis phase in the risk assessment.
- P&S helps **define** participants, purpose, and boundaries/direction of analysis.
- Products **include** problem statement, conceptual model, and analysis plan.

Questions?

Exposure Assessment for Air Toxics



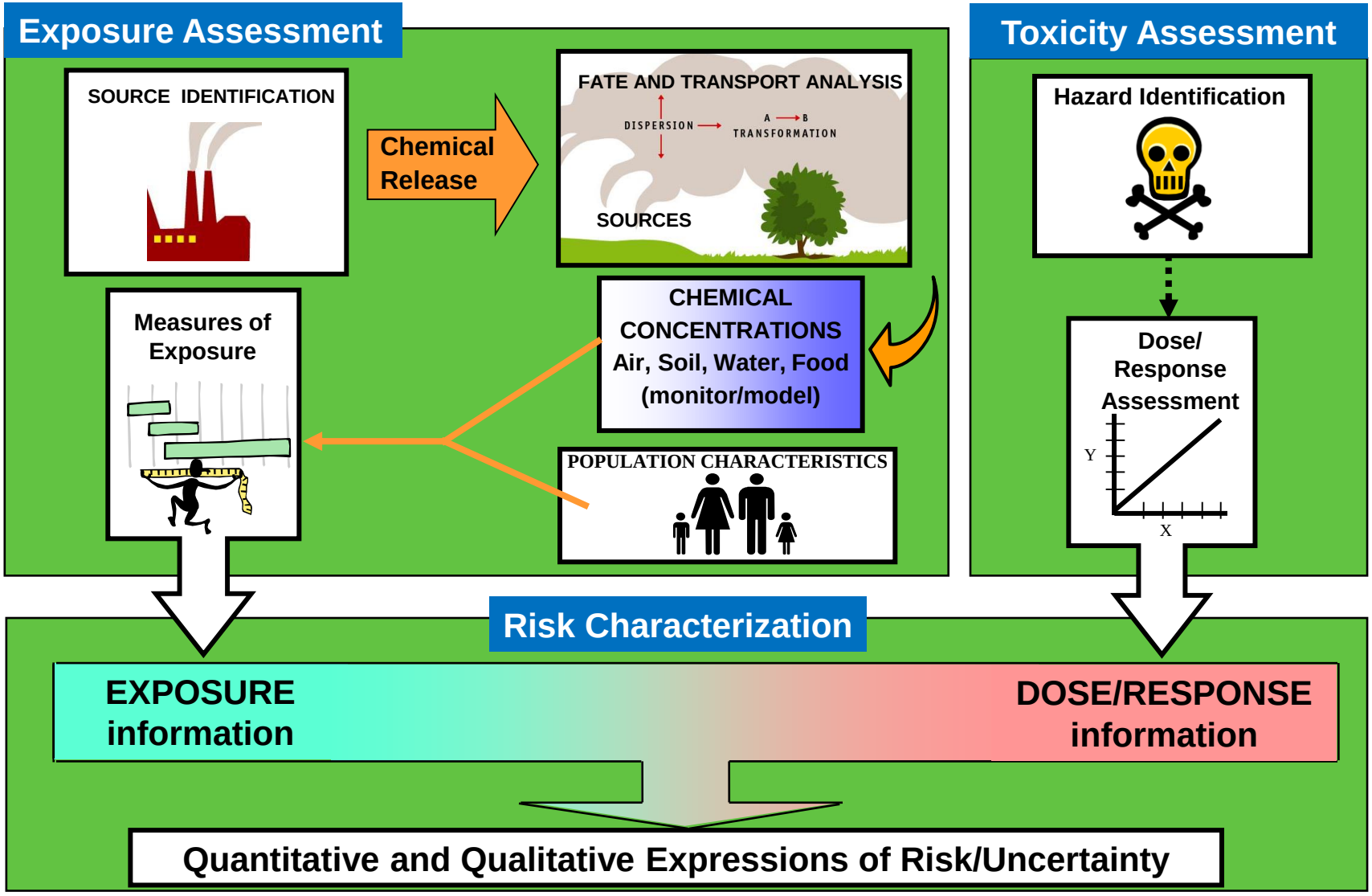
Risk Assessment: The Actual Process

Risk = f[(Measure of Exposure), (Measure of Toxicity)**]**

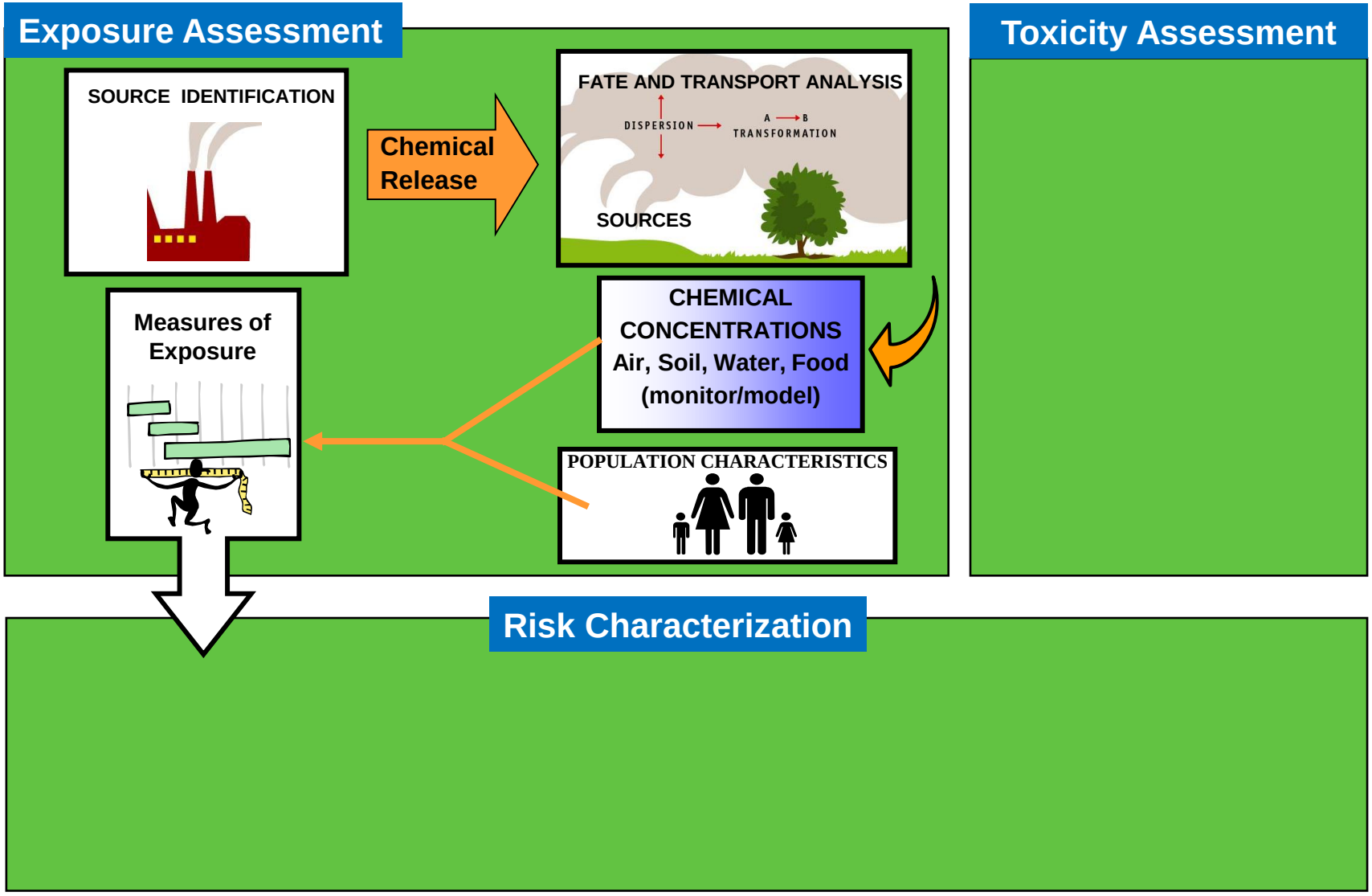
Who is exposed to a chemical?

How are they exposed to the chemical?

Detailed Air Toxics Risk Assessment Process: Planning and Scoping



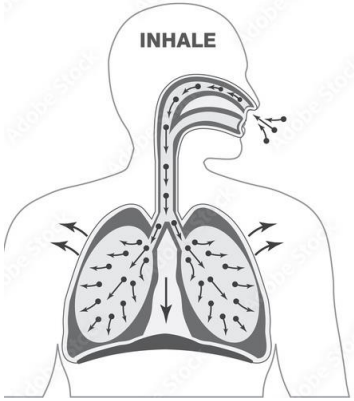
Detailed Air Toxics Risk Assessment Process: Planning and Scoping



What is Exposure?

Contact of a chemical with:

- Skin
- Mouth
- Nostrils
- Punctures in the skin



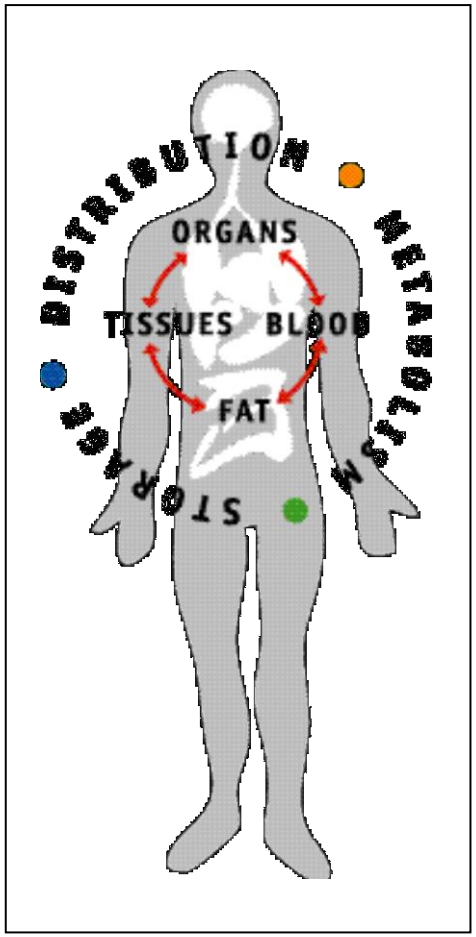
For air toxics human health risk assessments, we will usually focus on exposure to people by:

- Contacting contaminated air by **inhalation**
- Contacting contaminated soil, water, or food by **ingestion**

What happens once exposure occurs?

Once inhaled or ingested, various processes can occur (depending on the chemical):

- Toxic effect can occur at the initial point of entry in the body
  - e.g., the respiratory or digestive tracts
- Portal of entry effect
- Toxic effect can occur at a point(s) distant from the portal of entry



Different Time Frames

Chronic Exposure

Long term (years to lifetime) exposure to (usually) relatively low levels of contaminant

Chronic exposure may result in **chronic effects**

- cancer, chronic obstructive pulmonary disease, neurological problems, etc.

Acute Exposure

Short term (minutes, hours, days) exposure to (usually) relative high levels of contaminant

Acute exposure may result in **acute effects**

- from relatively mild (eye irritation), to extreme (asthma attack), to fatal

But we don't breathe in the same air all the time!

People do different activities in different microenvironments throughout various life stages:

- Going to school, work, shopping, etc.
- Going on vacation
- Time spent in the car
- Time spent in the home
- Time working in the yard
- Time away from home on work travel

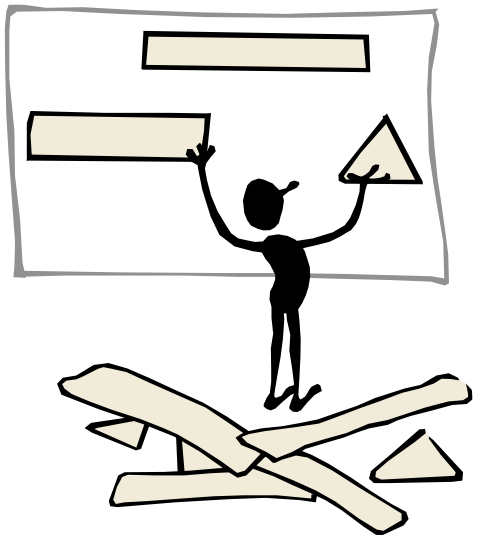
Exposure Assessment

For air toxics, Exposure Assessment is the process we go through to understand:

- Who is potentially exposed to air toxics
- What air toxics they are potentially exposed to
- How the chemicals get from the point of release to the point of exposure
- How the exposure occurs, possibly through multiple routes

Exposure Assessment: The Process

Develop a Study-Specific Conceptual Model



1. **Characterize the exposure setting**
   - Physical environment
   - Scale of the study area
   - Important sources and chemicals
   - Potentially exposed populations
1. **Identify exposure pathways**
   - Fate and transport of chemicals
   - Exposure points and routes

Exposure Assessment: The Process

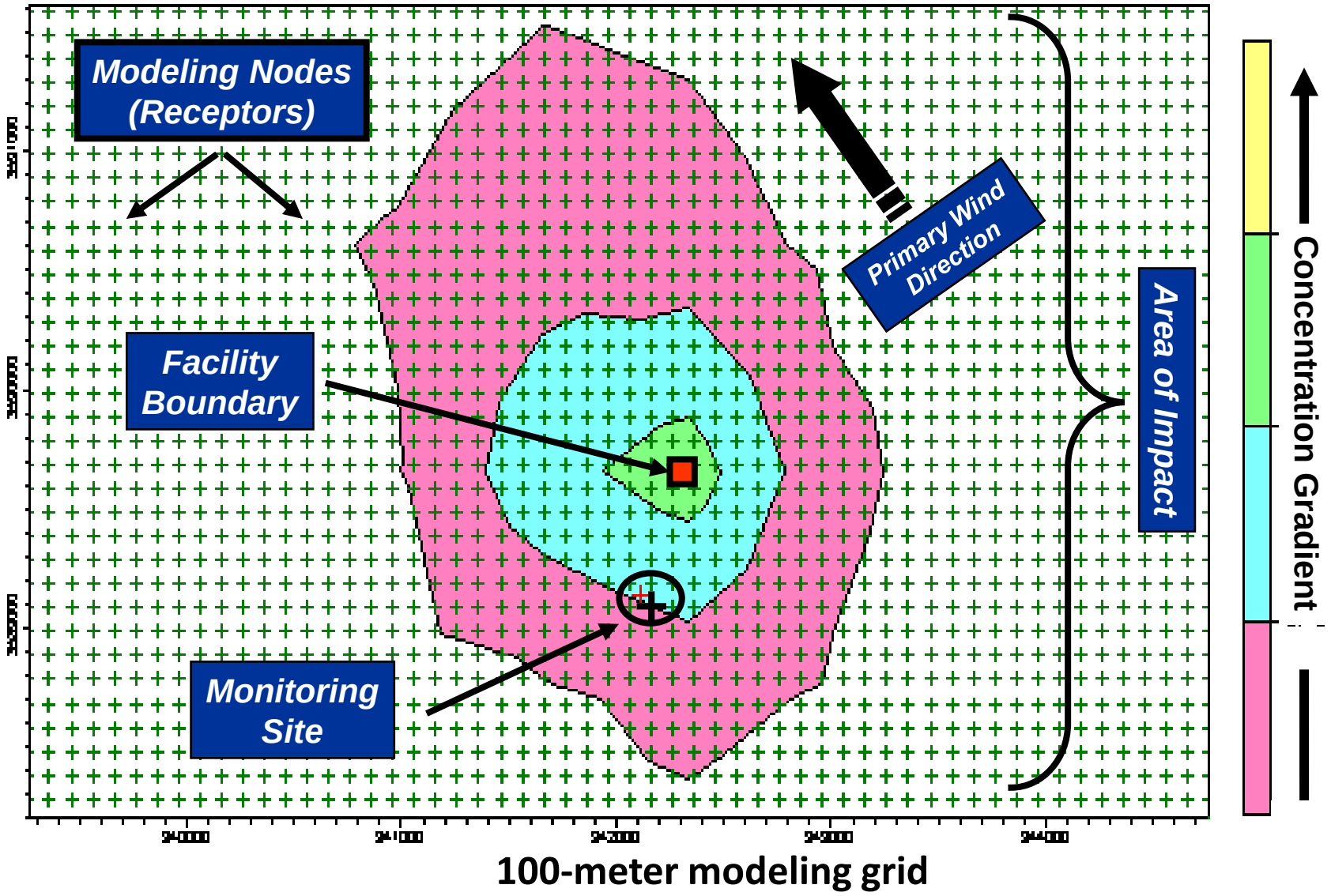
3. Quantify exposure

- Use monitoring or fate/transport modeling to estimate the chemical concentrations in air, water, soil, food at the point of contact (the **EC**)
  - The **EC** in air is the quantitative measure of exposure for **inhalation**
  - The **EC** in water, soil, food is used to calculate intake, the quantitative measure of exposure for **ingestion**
- May use exposure modeling to refine the estimate of exposure
  - e.g., an apparent **EC** for inhalation

How do we determine the exposure concentration?

An example
for the inhalation pathway

Air Dispersion Modeling and/or Air Monitoring



Questions?

Toxicity Assessment for Air Toxics

Risk Assessment: The Actual Process

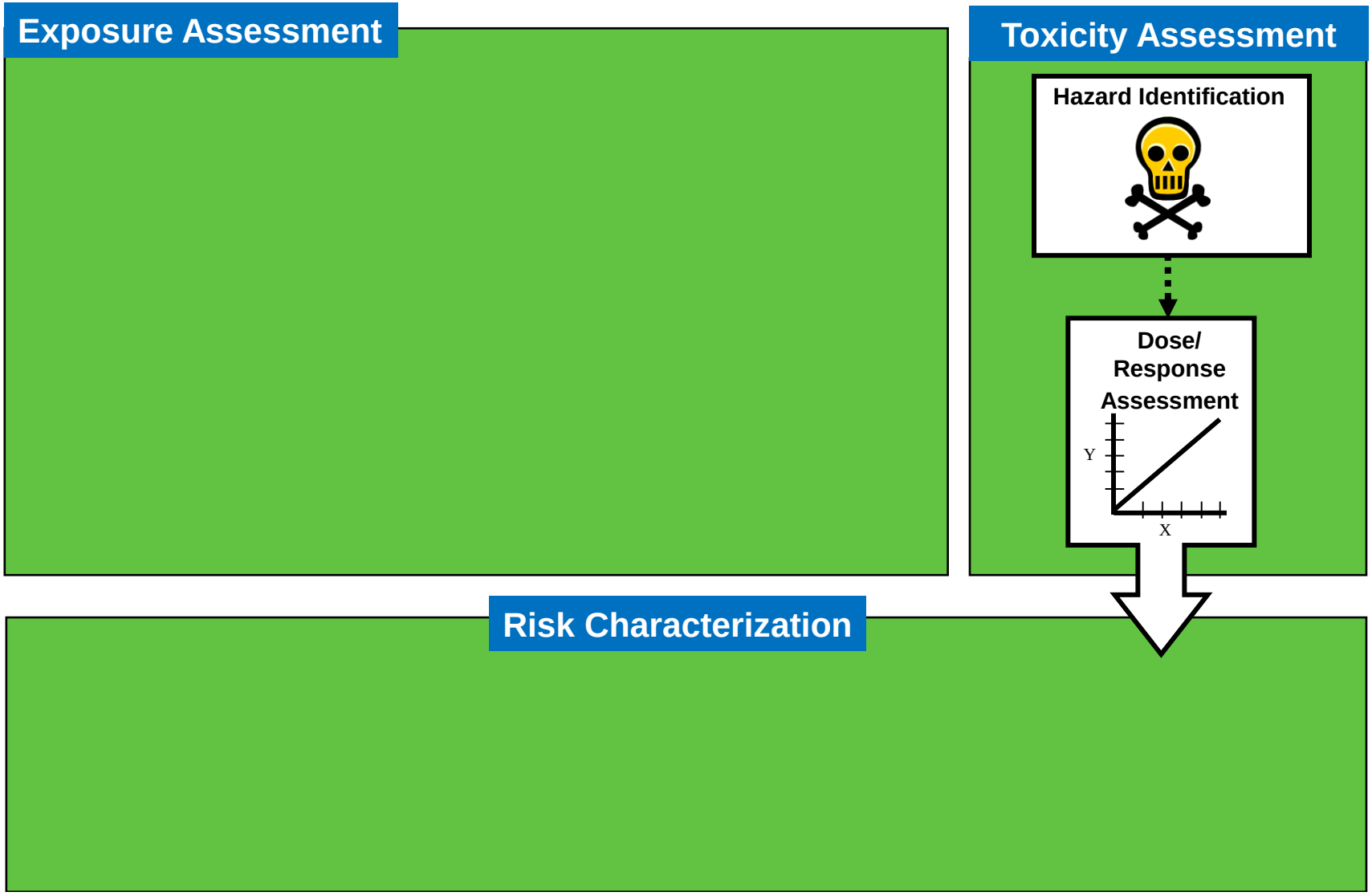
Risk = f[(Measure of Exposure), (Measure of Toxicity)]

2-Step Process:

1. **Hazard Identification**
   Is the chemical dangerous?

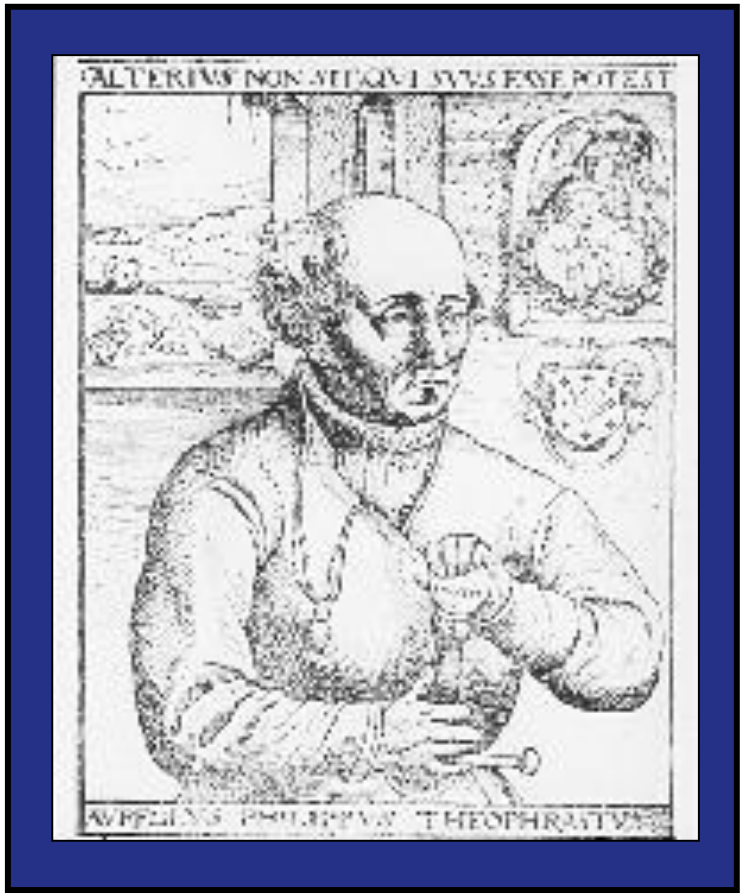
2. **Dose-Response Assessment**
   How potent is the chemical?
   … as a carcinogen?
   … for noncancer effects?

Detailed Air Toxics Risk Assessment Process: Planning and Scoping



All substances are poisons: there is none which is not a poison. The right dose differentiates a poison and a remedy.

- Paracelsus



The right dose, over the right time period, through the right route makes the poison.

-Paracelsus Updated

Step 1: Hazard Identification

- Is exposure to a chemical causally linked to particular health effects?
- Is the effect of practical significance?
- What is the nature and strength of the evidence of causation?

Numerous Biologic Endpoints

Non-Cancer

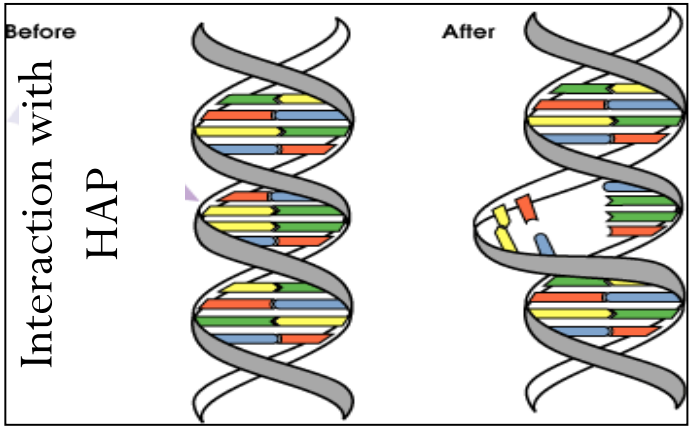
- Reproductive, developmental, neurological disorders
- Immunologic effects
- Acute effects (e.g., edema, CNS depression)
- Various other systemic effects (e.g., liver, kidney, lung damage)

→ Multiple Adverse Endpoints

Cancer

- Mutations
- DNA damage

→ Uncontrolled growth of cells

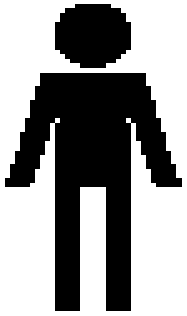


Hazard Identification

Where do we get our information?

Data on adverse biologic effects usually generated through:

- Epidemiological studies
- *In vivo* biologic assays
- *In vitro* assays
- Structure-activity relationships (SAR)



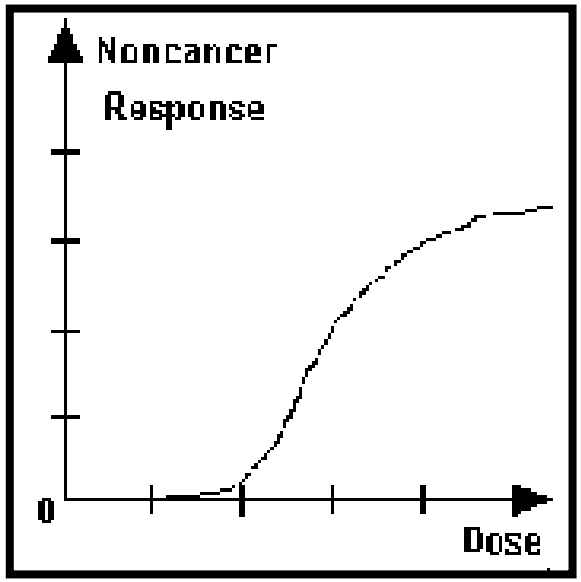
Human Epidemiological Studies

Laboratory Animal Experiments

Step 2: Dose/Response Assessment

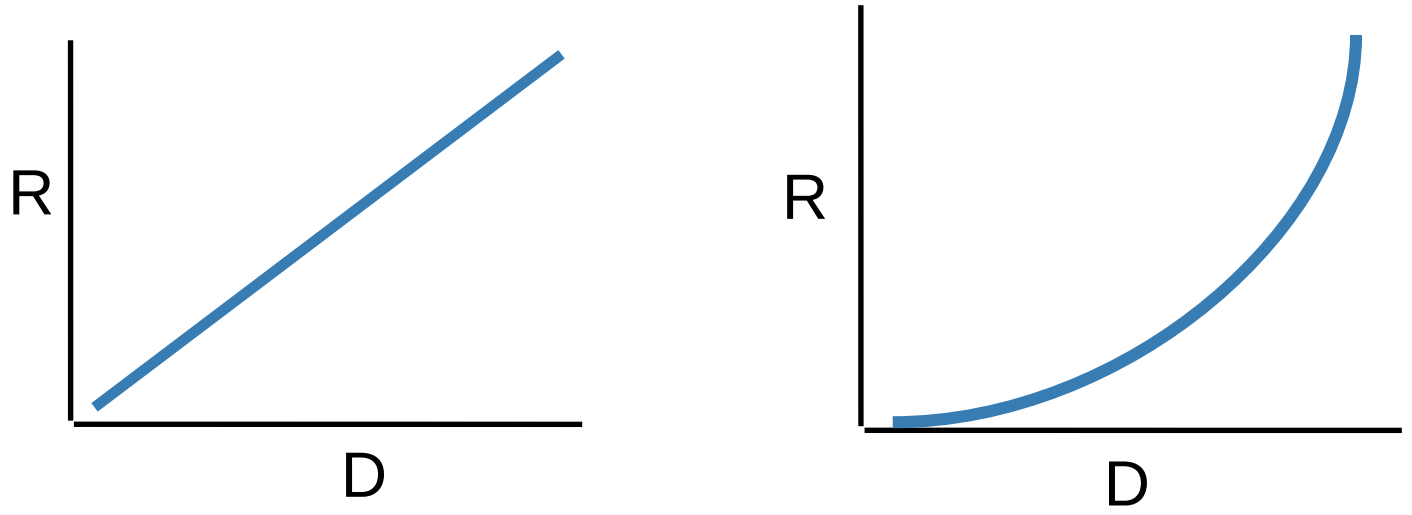
Now that we've established that a chemical is toxic –

- We need to understand how much dose gives how much response.
  - How potent is the chemical?
- Some of our Hazard ID information may help us answer that question.



Dose-Response Curves

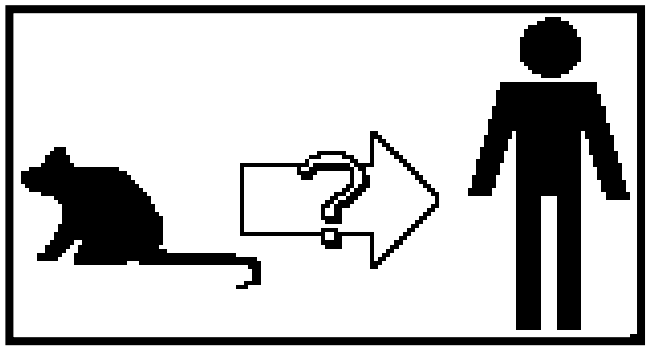
- Response patterns show how the compound affects exposed organisms
- Patterns can differ from one health endpoint to another
- Patterns can differ between populations (e.g. animals to humans, different life stages)



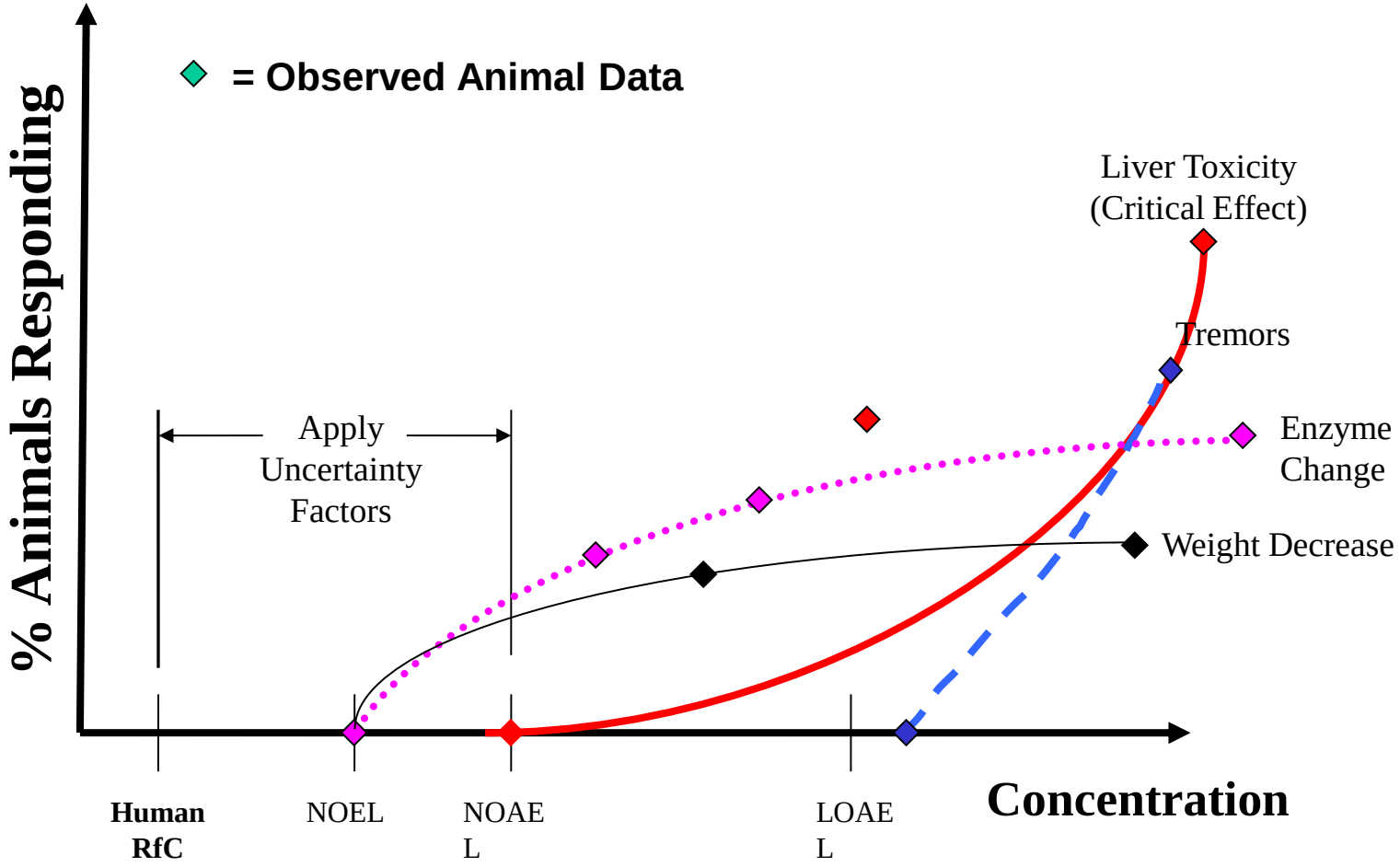
Dose-Response: Noncancer

EPA assumes:

- There is a threshold below which no observable adverse effect will occur (i.e., there is a toxicity threshold).
- We usually don't know exactly where that point is from our lab animal data.
    - So, we use our animal data, in conjunction with a series of uncertainty factors, to estimate a "safe" or "reference" exposure for humans.



Dose-Response: Noncancer



Inhalation Reference Concentraton (RfC)

$$RfC\,(mg/m^3) = \frac{NOAEL\ or\ LOAEL\ (HEC)}{UF_1\ x\ UF_2\ \ldots\ x\ UF_i}$$

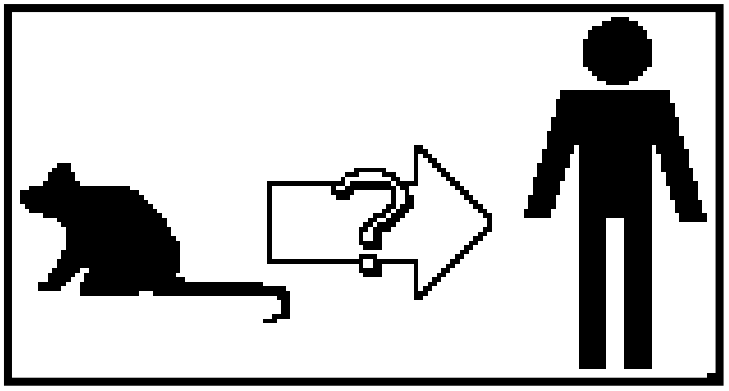
Uncertainty Factor Criteria	UF
• Extrapolating from animal data	10, 3, or 1
• Sensitive human populations	10, 3, or 1
• Subchronic NOAEL instead of chronic NOAEL	10, 3, or 1
• LOAEL used instead of NOAEL	10, 3, or 1
• Uncertainties in the database for the chemical	10, 3, or 1

- HEC = Human Equivalent Concentration
- RfD (Oral) calculated similarly (usually in mg/kg-d)
- Some RfCs developed in the past may have employed a modifying factor (MF) to account for overall quality of the tox database

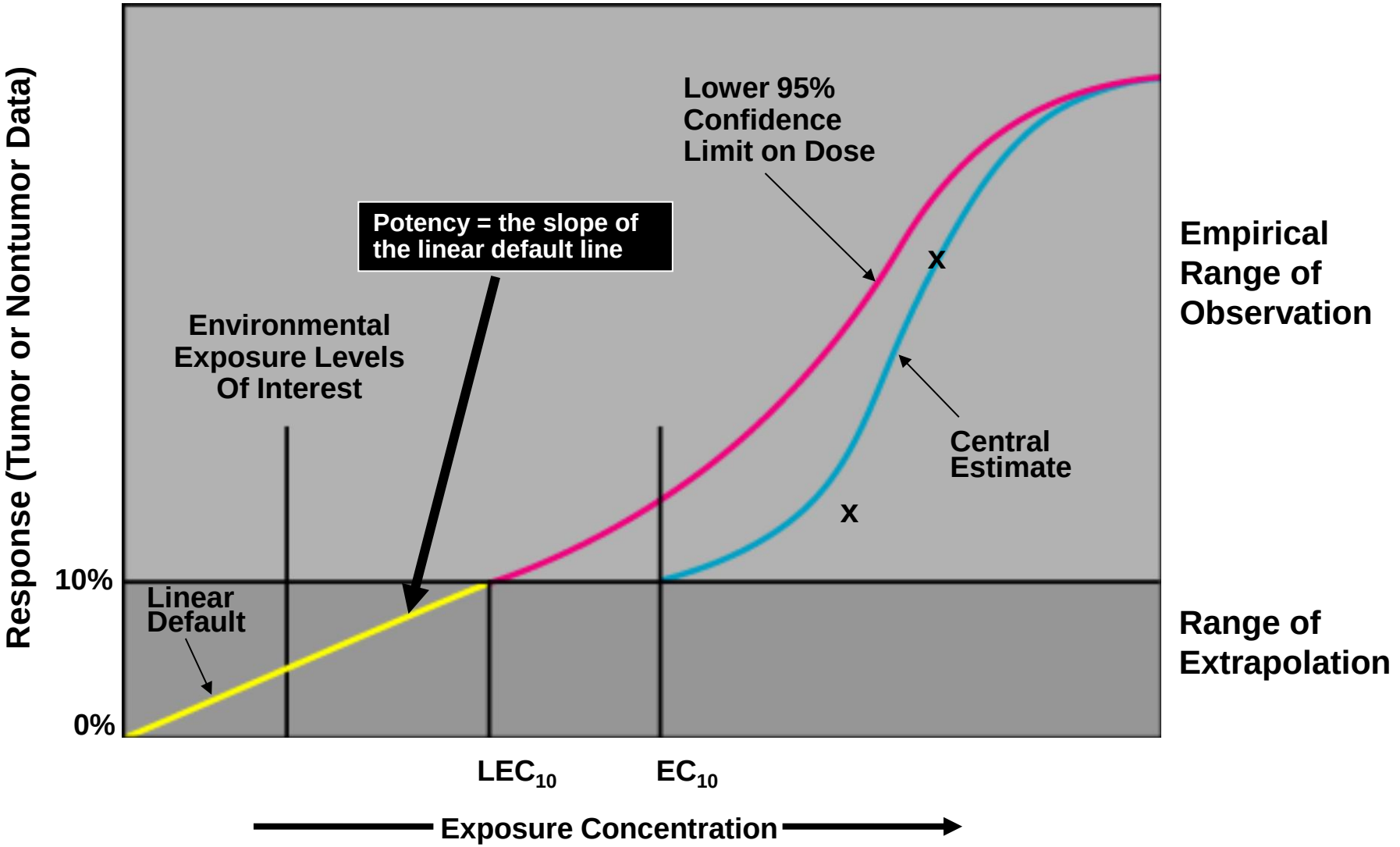
Dose-Response - Cancer

Unless we have data that indicates otherwise, we assume:

- There is **no exposure** which is without cancer risk (a non-threshold response).
  - Even very low doses are not risk free.
- We know the lowest exposure from our lab animal experiments, but how do we extrapolate to the very low concentrations people are more likely to experience?



Dose-Response - Cancer



Inhalation Unit Risk

IUR (risk per ug/m3) = Slope of the line from the point of departure to zero

- **IUR** is the unitless upper bound estimate of the probability of tumor formation per unit concentration of chemical
- **Measures of potency for ingestion** are developed in a similar fashion
  - However, in units of (risk per mg/kg-day)

Summary

Cancer Risk

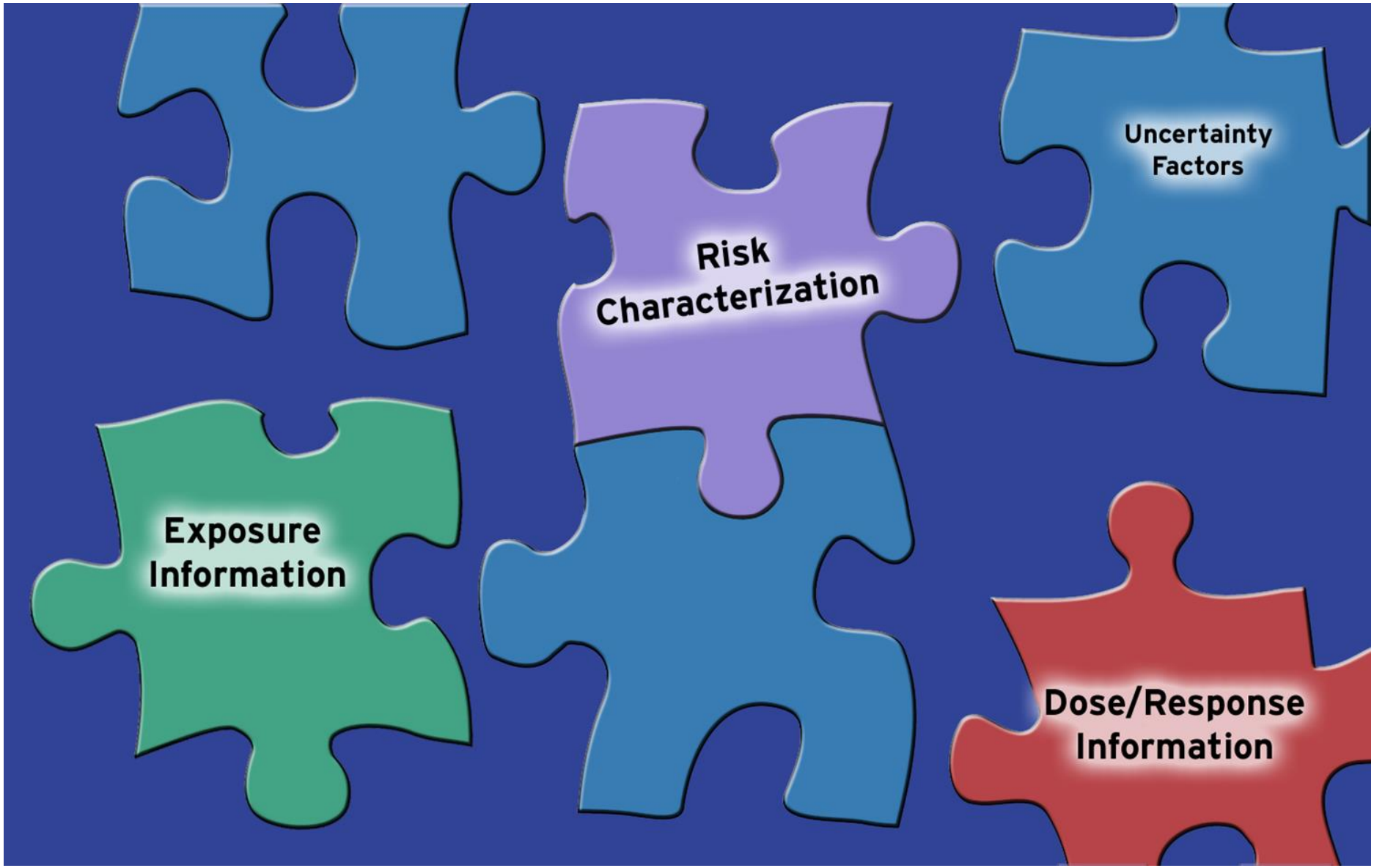
- Non-threshold (generally)
- Slope Factors
  - Inhalation Unit Risk
  - Oral Potency Factor

Non-Cancer Hazard

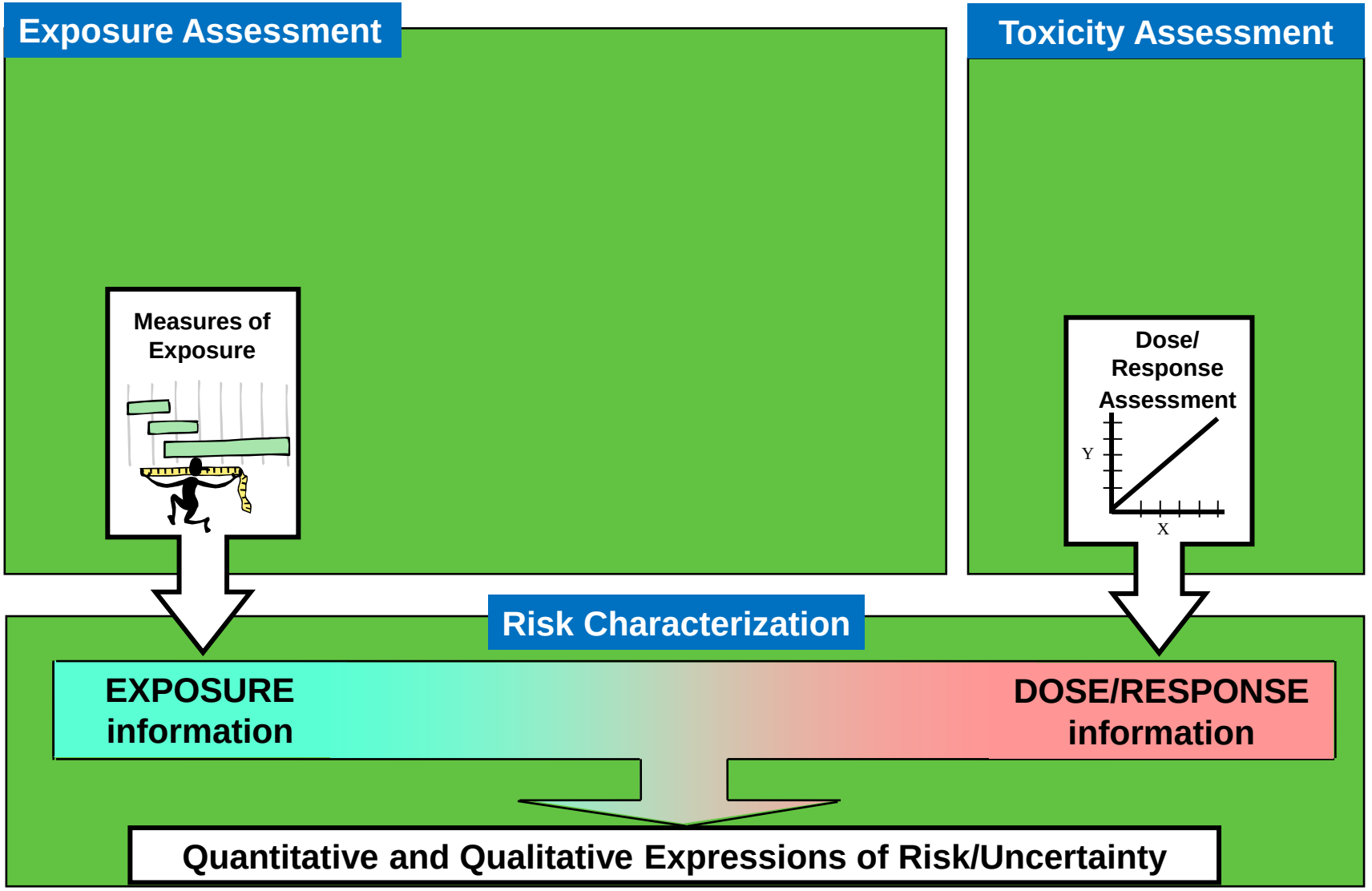
- Threshold (generally)
- Reference Values
  - RfC (inhalation)
  - RfD (oral)

Questions?

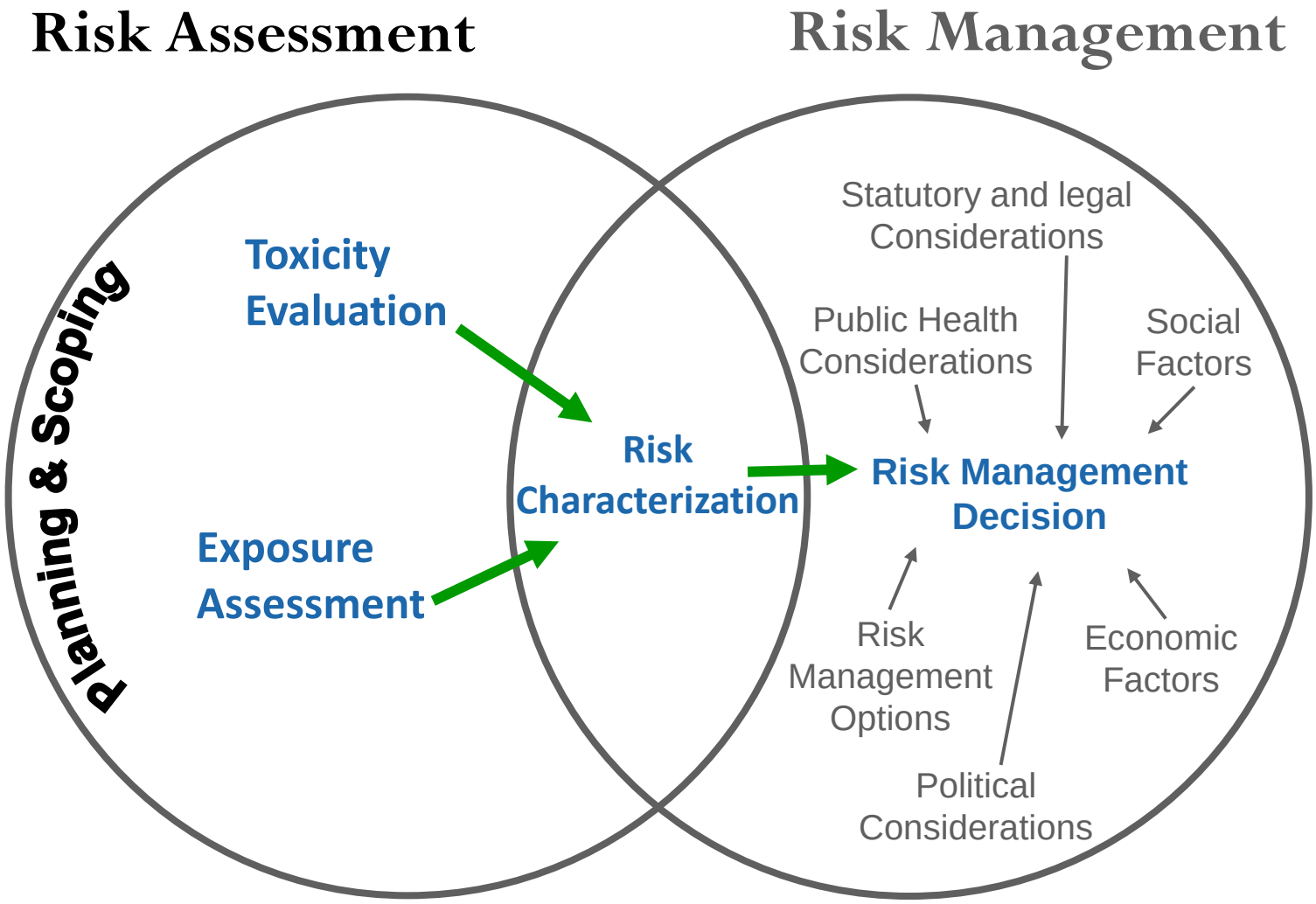
Risk Characterization for Air Toxics



Detailed Air Toxics Risk Assessment Process: Planning and Scoping

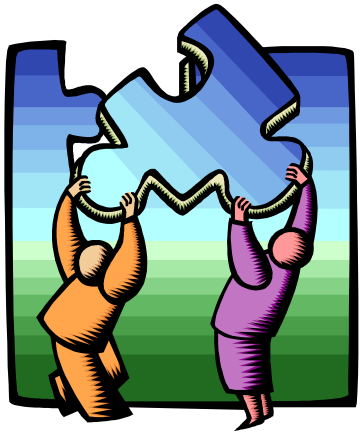


Why is risk characterization important?



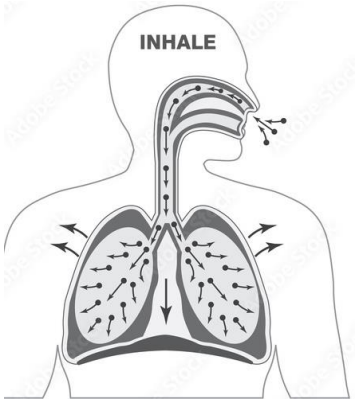
The Major Steps: Putting it all together

Review and combine the outputs from toxicity and exposure assessments



1. Quantify risks from individual chemicals for each pathway separately (e.g., inhalation, ingestion)
2. Combine risks from multiple chemicals **within** each pathway
3. Combine risks **across** exposure pathways to give total risk

Example: Multipathway Risk Characterization



Assess Exposure

Combine with Toxicity Data

Inhalation Pathway-Specific Risk

Assess Exposure

Combine with Toxicity Data

Ingestion Pathway-Specific Risk

+

Total Risk

Remember

We normally go through this entire process twice!

1. Calculate and present the risks posed by **cancer** causing chemicals **within** and then **across** pathways
2. Calculate and present the **noncancer hazards** posed by various chemicals **within** and then **across** pathways

Inhalation Cancer Risk

How do you calculate it?

The basic equation for calculating risk from breathing a carcinogenic air toxic is:

Risk = EC x IUR

where:

EC = Exposure Concentration = concentration of the chemical in air at the point of exposure (ug/m^3)

IUR = Inhalation Unit Risk ($risk/ug/m^3$)

Inhalation Cancer Risk

What happens when multiple carcinogens are present?

The equation is the same, however, you usually sum over all the different carcinogens present in the air:

$$\textbf{Risk} = (EC_1 \times IUR_1) + (EC_2 \times IUR_2) + \ldots (EC_i \times IUR_i)$$

where:

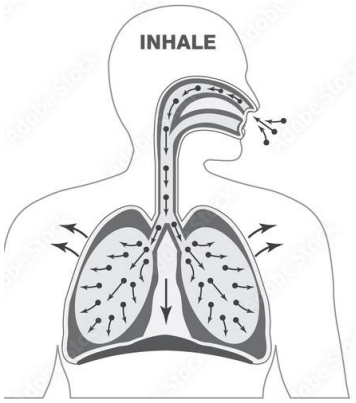
EC_i = concentration of the i^{th} chemical in the air at the point of exposure (ug/m^3)

IUR_i = Inhalation Unit Risk of the i^{th} chemical in the air ($risk/ug/m^3$)

Cancer Risk

What do the answers mean?

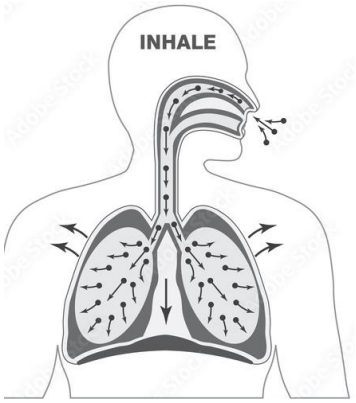
Cancer risk is a **probability** (e.g., $2x10^{-5}$) of an individual developing cancer because of the exposure in question.



Cancer Risk

What do the answers mean?

The answer you get is the **excess risk to an individual** at the point where “EC” is either measured (by monitoring) or estimated (by modeling).



Inhalation NonCancer Hazard

How do you calculate it?

The basic equation for calculating hazard from breathing an air toxic that causes a noncancer effect is:

Hazard Quotient = EC/RfC

where:

EC = Exposure Concentration = concentration of the chemical in air at the point of exposure (mg/m^3)

RfC = Reference Concentration (mg/m^3)

Inhalation Noncancer Hazard

What happens when multiple noncarcinogens are present?

The equation is the same, however, you usually sum over all the different noncarcinogens present in the air:

$$\textbf{Hazard Index} = (EC_1 / RfC_1) + (EC_2 / RfC_2) + \ldots (EC_i / RfC_i)$$

where:

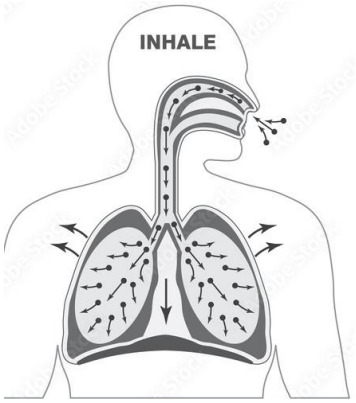
EC_i = concentration of the i^{th} chemical in the air at the point of exposure (mg/m^3)

RfC_i = Reference Concentration of the i^{th} chemical in the air (mg/m^3)

NonCancer Risk

What do the hazard answers mean?

The answer you get is the **hazard to an individual** at the point where “EC” is either measured (by monitoring) or estimated (by modeling).



TOSHI

If the initial Hazard Index (HI) calculation gives an HI ≥ 1:

- A target organ specific hazard index (TOSHI) may be warranted to clarify the potential impact of multi-chemical exposures on the exposed person
    - since not all chemicals affect the same organs or have the same mechanism of toxicity

A toxicologist with experience in this area should perform this analysis.

No Toxicity Data?

For chemicals with no toxicity data, possibilities are:

- Exclude from analysis and discuss as an uncertainty (most often done)
- Derive a toxicity value
  - **"From scratch"** using good-quality toxicological or epidemiological studies, accepted mathematical models
  - Use a **"surrogate"** toxicity value
    - i.e., a known toxicity value for another chemical that is thought to behave toxicologically like the chemical in question
  - Estimate a **"scaled value"** based on structure-activity relationship
    - e.g., toxicity equivalency factors (TEQs) for dioxin and certain PCB congeners

A toxicologist should perform these analyses.

Questions?