COOPERATIVE EXTENSION
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ES/RP 531
Fundamentals of Environmental Toxicology

Lecture 2

Risk Management &
Environmental Toxicology

Instructor: Allan Felsot
(afelsot@tricity.wsu.edu)

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Speaking the Same Language--Toxicity Terms

- Toxicity: innate potential of a substance to cause injury
- Hazard: potential to cause injury under a certain set of circumstances
- Safety: subjective term and therefore not definitive, but in the context of risk management it refers to the practical certainty that injury will not result from use of a substance under specified conditions of quantity and manner of use.
- Risk: probability (likelihood) of harm

Speaking the Same Language--Exposure Duration

- Acute: dose delivered in a single event (or over a short time interval); absorption rapid
  - For aquatic organisms, we refer to the length of time they are exposed (either 48 or 96 h is standard)
- Chronic: dose delivered over a period of time, with some defined frequency
  - For studies on terrestrial wildlife and aquatic organisms, chronic exposure encompasses a reproductive life cycle or period

Speaking the Same Language--Spectrum of Toxic Effects

- Time to Effect
  - Acute: effect occur or develop rapidly after a single administration of a substance
    - In environmental tox testing, acute effects are judged after acute exposure duration; usually death is the endpoint
  - Chronic: effects occur or develop after elapse of time
    - An acute exposure could result in chronic effects

Speaking the Same Language--Spectrum of Toxic Effects

- Site of Action Effects
  - Local: effects occur at site of first contact with the substance
    - Dermal irritations
  - Systemic: effects occur at a site distant to the site of absorption
    - Injury to soft tissue organs
    - Reproductive or nervous system effects

Speaking the Same Language--**Residues**

- The molecules of a substance once they are released into the environment and/or absorbed after exposure
  - The term is used to distinguish from the pure substance prior to environmental emission

Speaking the Same Language--Residue Concentrations

- Magnitude of residue is expressed as a concentration
  - Mass of substance per unit of volume, mass, or surface area
- Water: µg/L or mg/L
- Soil: µg/kg or mg/kg
- Surface Area: $\mu g/cm^2$ or mg/m^2
- Air: $\mu g/m^3$

Speaking the Same Language--Residue Concentrations

- Proportional concentration expressions
  - ppm, ppb, ppt
  - Should distinguish whether the proportion is given on a weight or volume basis,especially if the medium does not have a density of 1 gram/cubic centimeter; 1 cm^3 of water = 1 mL = 1 g)
    - 1 ppb of substance X in water is 1 µg/L (1 ppb w/v)
    - 1 ppb of substance X in soil is 1 µg/kg (1 ppb w/w)
- Proportional concentrations can be changed to percentages purity
  - 1 ppb of substance X in water means the water (from the perspective of X) has a purity of 99.9999999%

Speaking the Same Language--Dose

- Residues in the body are usually expressed as mg/kg (mammals and birds) or µg/kg (invertebrates and fish)
- Doses are expressed relative to body weight and normalized to the time interval of exposure
  - mg/kg/day
- For biochemical studies examining in vitro exposures, doses expressed as molar units
  - 1 molar dosage means exposure to the gram equivalent molecular weight of the substance in a liter of water

Environmental Toxicology--Goals

- Prediction of health and environmental effects from exposure to natural and synthetic xenobiotics
- Theoretical framework for making predictions given by environmental chemodynamic and pharmacodynamic theory
  - Works fairly well at the level of the individual
  - Primitive understanding in translating the individual effects to higher levels of organization
- Nevertheless, we still want to manage the risk
  - Manifested through the regulatory process

Risk Assessment (RA)

- The term risk itself refers to the probability (likelihood) that adverse effect will be manifested given specific conditions of exposure and dose
- Note that probability is really a mathematical concept and can never be zero, but only approach it

RA Defined from Different Perspectives

- NRC 1989: "characterization of the potential adverse effects of exposures to hazards" *("Improving Risk Communication")*
- NRC 1994: "..evaluation of scientific information on the hazardous properties of environmental agents and on the extent of human exposure to those agents. The product of the evaluation is a statement regarding the probability that populations so exposed will be harmed, and to what degree." *("Science & Judgment in Risk Assessment")*
  - May be qualitative or quantitative

Risk Assessment (RA)-- Operational Definitions

- What are the hazards of concern as a consequence of a substance or activity?
- What is the probable exposure to each hazard in total number of people or valued things?
- What is the probability of each type of harm from a given exposure to each hazard?
- What is the distribution of exposure?

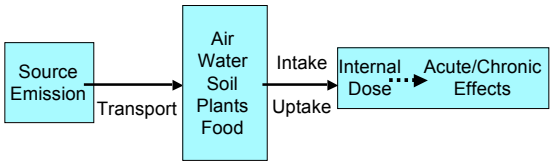
NRC 1989
"Improving Risk Communication"

Risk Assessment (RA)-- Operational Definitions

- What are the sensitivities of different populations of individuals to each hazard?
- How do exposures interact with exposures to other hazards?
- What are the qualities of the hazard?
- What is the total population risk, taking into account all of the above questions?

NRC 1989
"Improving Risk Communication"

The Source to Organism Scenario Analyzed by Risk Assessment



•1994 NRC report, *"Science & Judment in Risk Assessment"*

Risk Assessment: Four Essential Analytical Steps

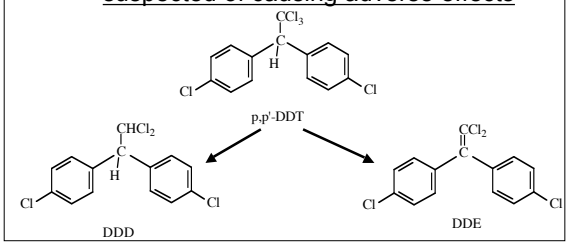
- Hazard Identification
- Dose-Response Assessment
- Exposure Assessment
- Risk Characterization

• First elucidated in the 1983 NRC report, *"Risk Assessment in the Federal Government"*

• Further refined in the 1994 NRC report, *"Science & Judment in Risk Assessment"*

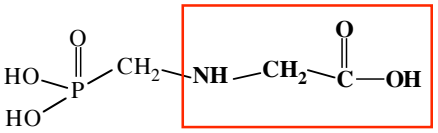
Hazard Identification

- Identification of contaminants suspected of causing adverse effects



Hazard ID

- Chemical structure can reveal a lot about potential metabolic pathways and likelihood of effect



glyphosate

Hazard Identification

- Identification of chemical would encompass a knowledge of its environmental chemodynamics (useful for eventual exposure assessment), but also its pharmacodynamics (PD) and pharmacokinetics (PK)
  - Physicochemical properties, for ex. water solubility can tell a lot about what might happen to the chemical in the environment and in the body
- Quantification of concentrations in the environment
  - Will consider this aspect as exposure assessment
  - Models can be built to predict bioconcentration from environmental concentrations

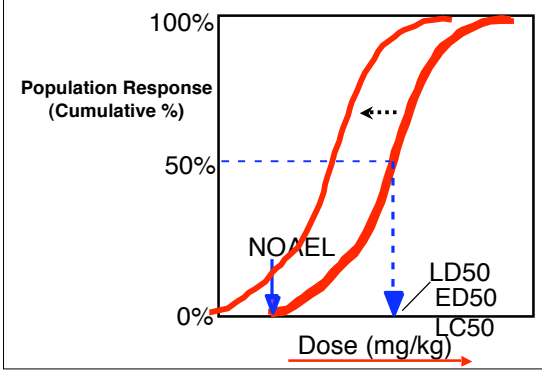
Hazard Identification

- Description of the specific forms of toxicity and an evaluation of the conditions under which these forms of toxicity might be expressed after exposure
  - Reliance on experimental studies
  - For human, environmental epidemiological evidence might be informative but its reliability and accuracy is very uncertain when dealing with the general population (as opposed to a special population, such as workers in a specific industry)

Dose-Response Assessment

- An evaluation of the conditions under which the toxic properties of a chemical might be manifested in exposed organisms
- Elucidation of the quantitative relationship between the dose and the toxic response
- Assessment of variations in response

"Dose Makes the Poison"



Exposure Assessment

- Specification of the population that might be exposed to the xenobiotic
  - For example, when EPA assesses dietary, drinking water, and residential exposure to pesticide residues, the agency uses population subgroups
    - Infants
    - 1-6 yrs
    - Teenager
    - Nursing Mothers
    - General U.S. population
  - Invertebrates, fish, birds
  - Endangered species present or not?

Exposure Assessment

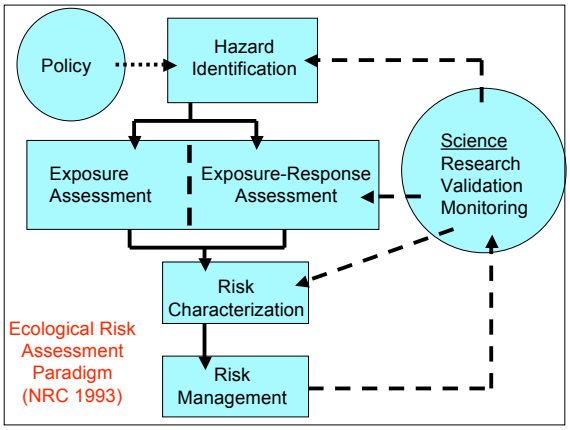
- Identification of exposure routes
  - Water, soil, plant foliage, seeds
- Timing, magnitude, and duration

Risk Characterization

- Integration of information from hazard id, dose-response, and exposure assessment to develop a qualitative or quantitative estimate of the likelihood that hazards of the xenobiotic will be manifested in exposed organisms
  - Note that in practice, estimation of risk is still based on individual responses
  - With reproductive rate information, and information about demographic characteristics, response of wildlife populations might be estimated
- Discussion of uncertainties

Human RA vs. Ecological RA

- The currently used RA paradigm was developed for human health assessments
- During 1989, a panel was assembled by the National Academy of Sciences (NAS) to determine the applicability to ecological risk assessment
  - Report summarized in NRC 1993 *("Issues in Risk Assessment")*
  - The conclusion found the paradigm usable but with some exceptions



Ecological Risk Assessment Paradigm (NRC 1993)

Some Unique Features of Ecological Risk Assessment

- Hazard ID should consider whether health or ecological effects are of sufficient importance to warrant further scientific study or immediate management action
- Responses in eco RA also include indirect effects, such as secondary poisoning of raptors, habitat changes that affect population (as opposed to direct mortality), etc.
- Exposure could include non-chemical stressors
  - For ex., vegetation control might subject frogs to more mutagenic UV light

Risk Management

- The purpose of characterizing risk is to help make a decision as to what we should do about it, or whether it is worth doing anything
- Much of the risk assessment activity stems from regulatory mandates imposed through statutory law
- Risk assessors range from industrial scientists to university faculty to consultants to government-employed regulators

Risk Management Activities

- Risk control assessment (NRC 1989)
  - What are the alternatives that would prevent the hazard(s) in question?
  - What are the risks of alternative actions and of a decision not to act?
  - What is the effectiveness of each alternative?
  - What are the costs of each alternative?
- Use of RA to develop priorities for management and regulation (strategic planning and priority setting)
- Note that RA is not the endpoint; decisions must be made on how to implement risk reduction, if necessary

Manifestations of Risk Mgt.-- Statutory Laws & Regulations

- Congresses passes laws (statutes) mandating executive agences (EPA, DOI, FDA, etc.) to create policies and rules that meet the mandates
  - The policies and rules become common law, a.k.a. regulations
- Note that RA is not completely an empirical (scientific) process because regulatory policies can influence course of the RA as well as define risk characterization

Statutory Laws Requiring Environmental Toxicology Expertise for Risk Assessment

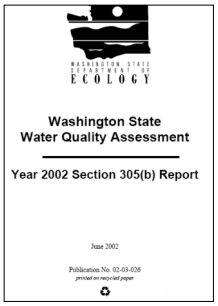
- FIFRA (Federal Insecticide Fungicide & Rodenticide Act of 1947)
  - Amended numerous times, but the 1972 FEPCA (Federal Environmental Pesticide Control Act) amendment changed the focus from human health to environmental health
    - Instituted the reasonable certainty of no harm standard prior to pesticide registration
  - Prior to pesticide registration, comprehensive risk assessments are done for human health effects (HED) and ecological fate and effects (EFED)

Statutory Laws Requiring Environmental Toxicology Expertise for Risk Assessment

- Clean Water Act
  - Statutory goal is to ensure water fishable, swimable, and navigable
  - Toxics discharge control
    - Point Source: National Pollution Discharge Elimination System Permits
    - Priority Pollutants List Criteria
    - Guidance criteria for protection of aquatic biota
    - Lists of impaired waters
    - Nonpoint source controls
    - Total Maximum Daily Loads (TMDLs)

http://www.epa.gov/305b/

http://www.ecy.wa.gov/biblio/0203026.html



Every two years, the States submit their water quality assessment reports to the EPA. EPA issues a biennial report to Congress on WQ in the U.S.

Statutory Laws Requiring Environmental Toxicology Expertise for Risk Assessment

- Toxic Substances Control Act
  - PMN (Premanufacturing Notification Rule, Section 5)--applicable to new products or new use of older products
    - Data must be submitted to EPA to show that manufacture, processing, distribution in commerce, use, and disposal of chemical substances will not present an unreasonable risk of injury to health or the environment
  - Section 8 mandates submission of health and safety studies and any information about the substance that indicates a substantial risk of injury to health or the environment

Statutory Laws Requiring Environmental Toxicology Expertise for Risk Assessment

- Superfund (SARA, Superfund Amendments & Reauthorization Act)
  - 1986 Amendment to the original "hazardous waste law", CERCLA (Comprehensive Environmental Response, Compensation, and Liability Act)
  - Among other provisions, increased the focus on human health problems
  - Required EPA to revise the Hazard Ranking System to ensure that it accurately assessed the relative degree of risk to human health and the environment posed by uncontrollable hazardous waste sites

Risk Management Devices

- **Narrative Standards**
  - Statement of desired objective or goal
    - "Do Not Drift…."
    - "No toxicity…"
    - City of Seattle Pesticide Use Reduction Strategy
      - "It is the policy of the City of Seattle to promote environmentally sensitive landscape pest and vegetation management by phasing out the use of the most hazardous pesticides and reducing overall pesticide use while preserving landscape assets and protecting the health and safety of the public and our employees."

Risk Management Devices

- **"Acceptable" Margins of Exposure (MOE) or Safety (MOS)--Numerical Standards**
  - **Hedging your bets with safety factors**
  - **"Codified" as numerical standards**
    - MCLs (Maximum Contaminant Levels)
    - Ambient Water Quality Criteria for Protection of Aquatic Organisms
    - Reference Doses (RfDs)
    - Population Adjusted Doses (PADs)

Risk Management

- Deciding what is tolerable and what to do to make a situation tolerable
- Hedging your bets with safety factors
  - Margins of Exposure

$$MOE = \frac{NOAEL}{Exposure}$$ Must be >100

  - Reference Doses

$$RfD = \frac{NOAEL}{100}$$ Must not exceed

  - Population Adjusted Doses

$$PAD = \frac{RfD}{10}$$ Must not exceed