8.4 ENVIRONMENTAL HEALTH AND TOXICOLOGY

College Board Topics 8.12 and 8.13

Related Reading Chapter 14, pages 374 - 384

Learning Objectives and Essential Knowledge

ENDURING UNDERSTANDING

EIN-3

Pollutants can have both direct and indirect impacts on the health of organisms, including humans.

LEARNING OBJECTIVE

EIN-3.A

Define lethal dose 50% (LD_{50}).

ESSENTIAL KNOWLEDGE

EIN-3.A.1

Lethal dose 50% (LD_{50}) is the dose of a chemical that is lethal to 50% of the population of a particular species.

SUGGESTED SKILL

Mathematical Routines

6.A

Determine an approach or method aligned with the problem to be solved.

ENDURING UNDERSTANDING

EIN-3

Pollutants can have both direct and indirect impacts on the health of organisms, including humans.

LEARNING OBJECTIVE

EIN-3.B

Evaluate dose response curves.

ESSENTIAL KNOWLEDGE

EIN-3.B.1

A dose response curve describes the effect on an organism or mortality rate in a population based on the dose of a particular toxin or drug.

SUGGESTED SKILL

Data Analysis

5.E

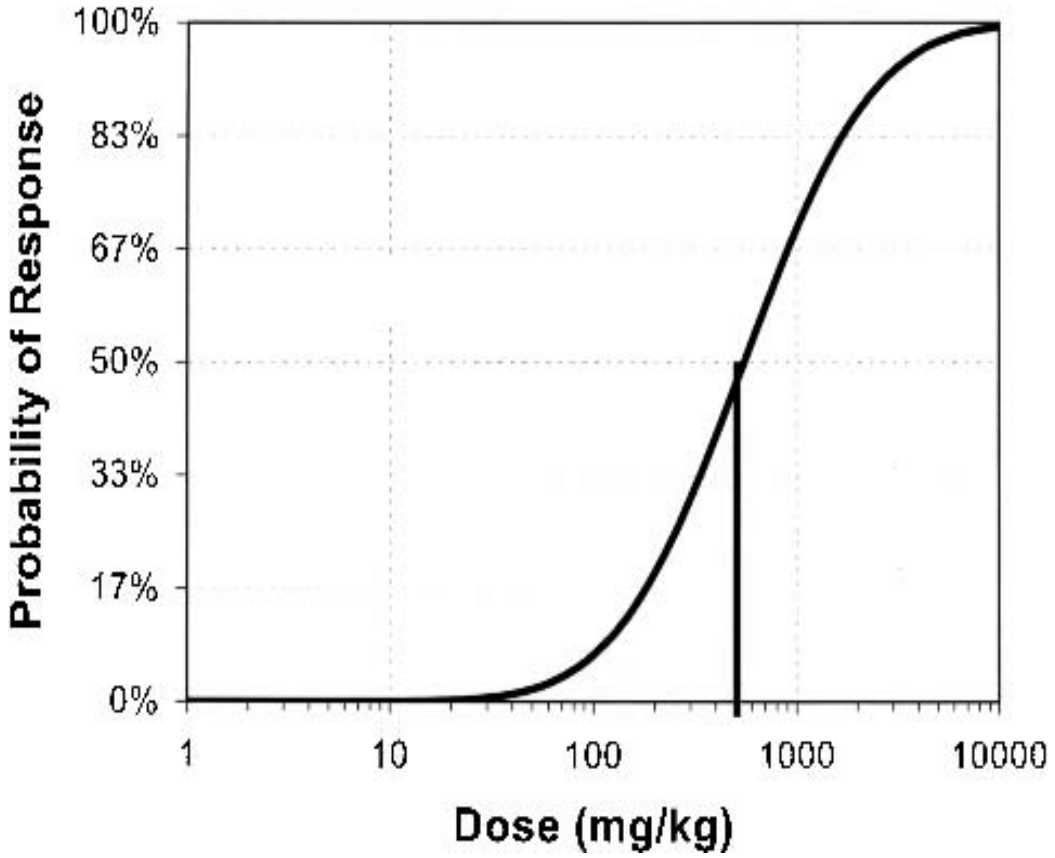
Explain what the data implies or illustrates about environmental issues.

Studying the effects of hazards

- Research into environmental health risks and the toxic effects of specific substances rely on:
  - ***Case histories***: The response of people who have been exposed to a substance in the past.
    - Most case history data comes from autopsies of those who have experienced ***acute*** exposures.
    - Little case history data exists for rare or new toxins and case history evidence rarely exists for low level exposures over long periods of time (***chronic exposure***).
    - Case histories tell us little about the risk of being exposed to a toxin.
  - ***Epidemiological studies***: large-scale, long term study of a group who have been exposed to a hazard vs. another group with no exposure. Statistical methods are used to look for significant differences between the groups. Natural experiments based on past accidents.
    - Monitoring survivors of Fukishima Nuclear meltdown and looking for evidence of thyroid cancers compared to the general population of Japan.
    - Subjects in epidemiological studies may be exposed to more than one risk factor, creating confounding variables which make it difficult for researchers to demonstrate cause and effect. (What if Fukishima survivors are also smokers?)
    - Epidemiological studies require a long wait time for results and do not provide information about the toxicology of new substances.
    - Epidemiological studies do provide accurate predictions of risk associated with exposure.
  - ***Animal studies*** performed in the controlled conditions of a laboratory provide specific data on the toxicity of substances.

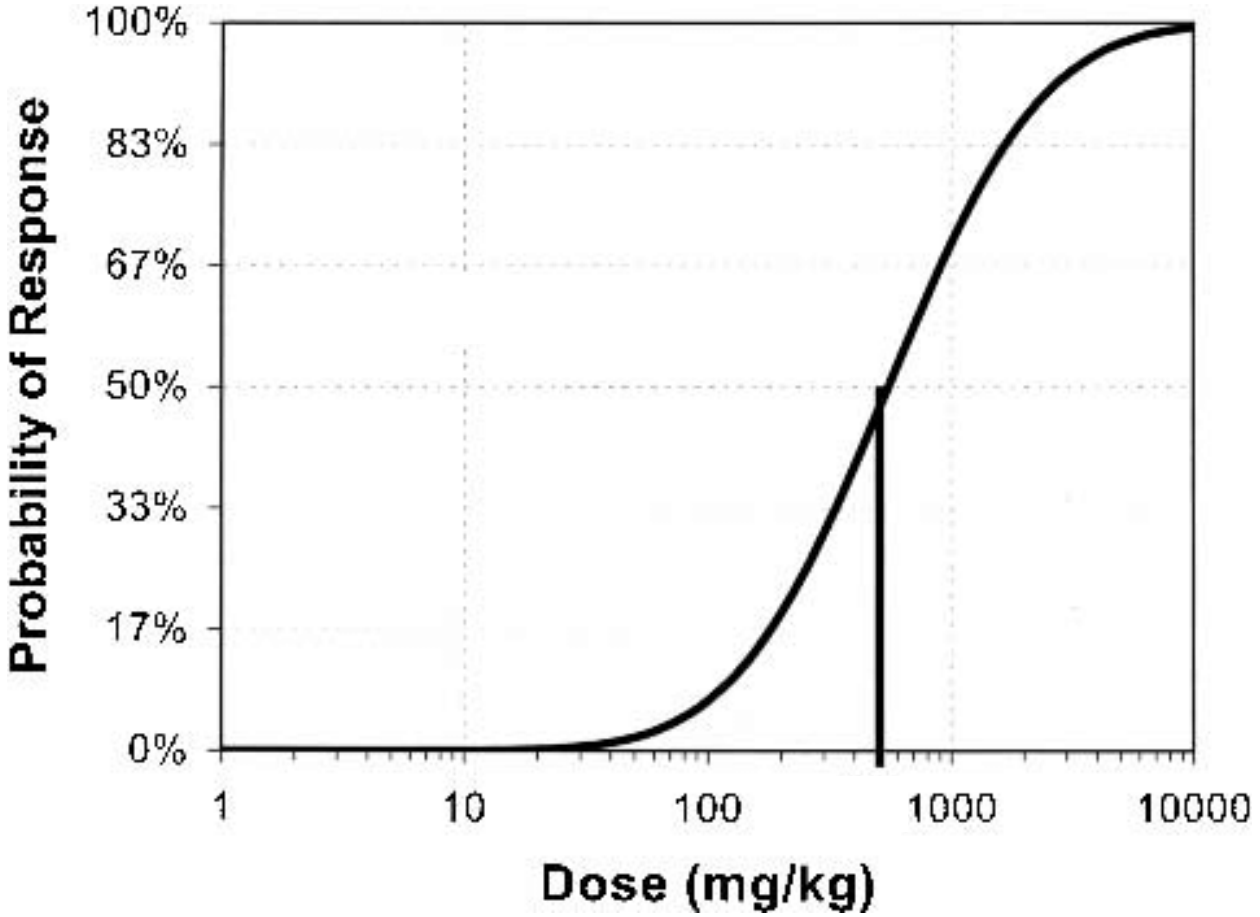
Animal testing uses dose-response analysis to determine establish causation and toxic effects.

- Human responses are often determined from animal studies with mice or rats.
  - Mammals share evolutionary history, so substances that harm rats and mice probably harm us.
- ***Dose-response analysis*** exposes groups of organisms to different concentrations (doses) of a chemical in order to measure the response (effect).
  - Independent variable = concentration of the chemical (added to food, water, or air)
  - Dependent variable = % of population showing a specified response (usually death or a specific impairment)
  - Results are plotted on a graph to create a ***dose-response curve*** that shows the probability of a specific effect at a given dose.

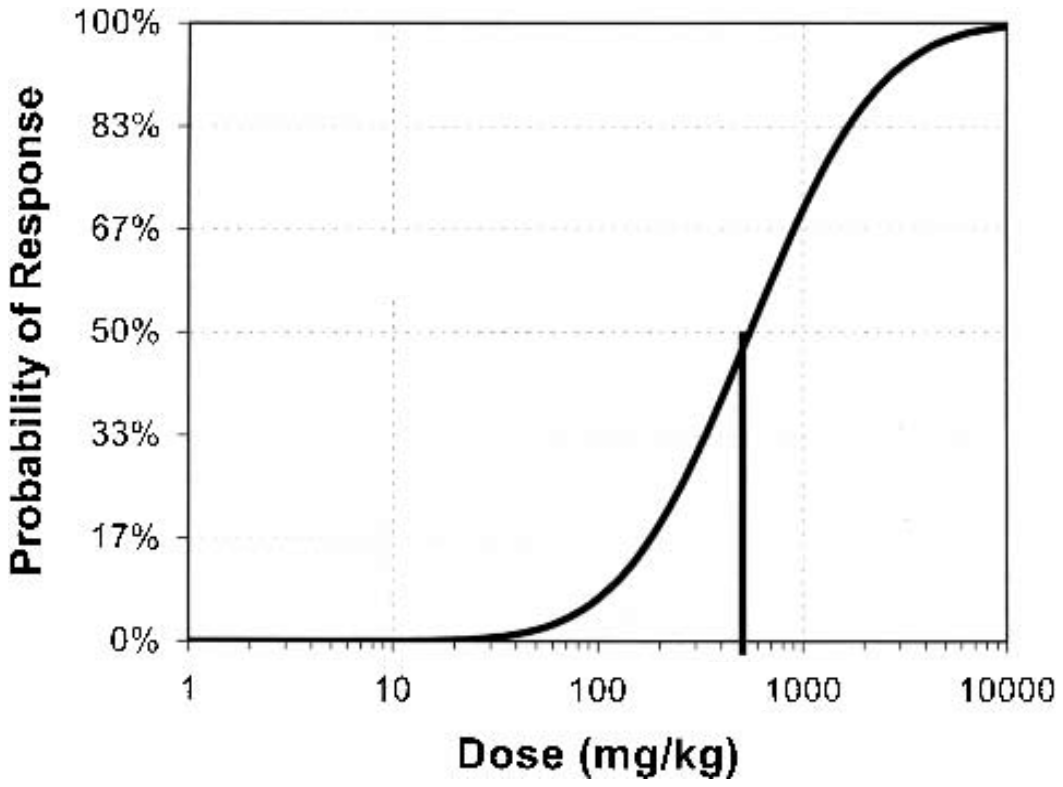


Interpreting dose-response curves

- Doses of toxins are usually measured as concentrations of the toxin added to food, water, or air.
  - Mass of toxin / unit of body mass (***mg/kg***)
  - Mass of toxin / volume of water, air, etc (***mg/L***)
  - The common units shown above also can be represented as ***parts per million (ppm)***
    - A mg is 1/1,000,000 of a kg
    - Since the density of water is 1 g/ml, a liter of water has a mass of 1000 grams. Therefore a mg/L is the same as 1 mg/1000g or 1 ppm.
    - 1 ppm = 1000 ppb (parts per billion)
- Toxins are often tested over a very wide range of concentrations.
  - Often requires a logarithmic scale on the x-axis.



Interpreting dose-response curves



- Dose response curves are usually "S-shaped"; low mortality at low doses, rapid increase in mortality as dose increases, level off near 100% mortality at high dosage
- The dose that causes a specific effect in 50% of the population is used as a common measure of toxicity.
  - LD_{50} : the dose or concentration of the chemical that kills 50% of the population being studied.
  - TD_{50}: the dose required to show a specific toxic effect in 50% of the population
  - ED_{50}: the dose required to show a specific, often beneficial effect, on 50% of the population.
  - Similar to TD_{50}, but ED_{50} is often reported when a substance results in a desired effect (the ED_{50} of a new medicine)
- ***Threshold dose*** is the minimum dosage where a specified response starts to occur
  - Cells/tissues/organs can metabolize or excrete low doses of a toxicant and impacts start to show at higher dosages.

Applying animal test data to humans presents challenges

- Dose-response studies with animals often use much larger doses, relative to the animals body size, than humans would be likely to experience in the environment.
  - Ensures that a response can be detected and that differences in response between large and small doses are apparent.
- Once a dose-response curve is constructed, researchers can extrapolate downward to estimate responses to even lower doses.
  - Allows estimation of doses that would cause a response in ever smaller portions of the animal population.
  - Such extrapolation is beyond the range of the data and introduces experimental uncertainty (1).
- A second extrapolation is required to apply animal data to humans due to our larger body size
  - This introduces a second extrapolation and increases uncertainty further (2).
- Test organisms and humans both show variation in their response to a toxin, introducing even greater uncertainty (3).
  - Affected by genetics, surroundings, etc.
  - People in poor health are more sensitive
  - Sensitivity also varies with sex, age, and weight
  - Fetuses, infants, and young children are more sensitive

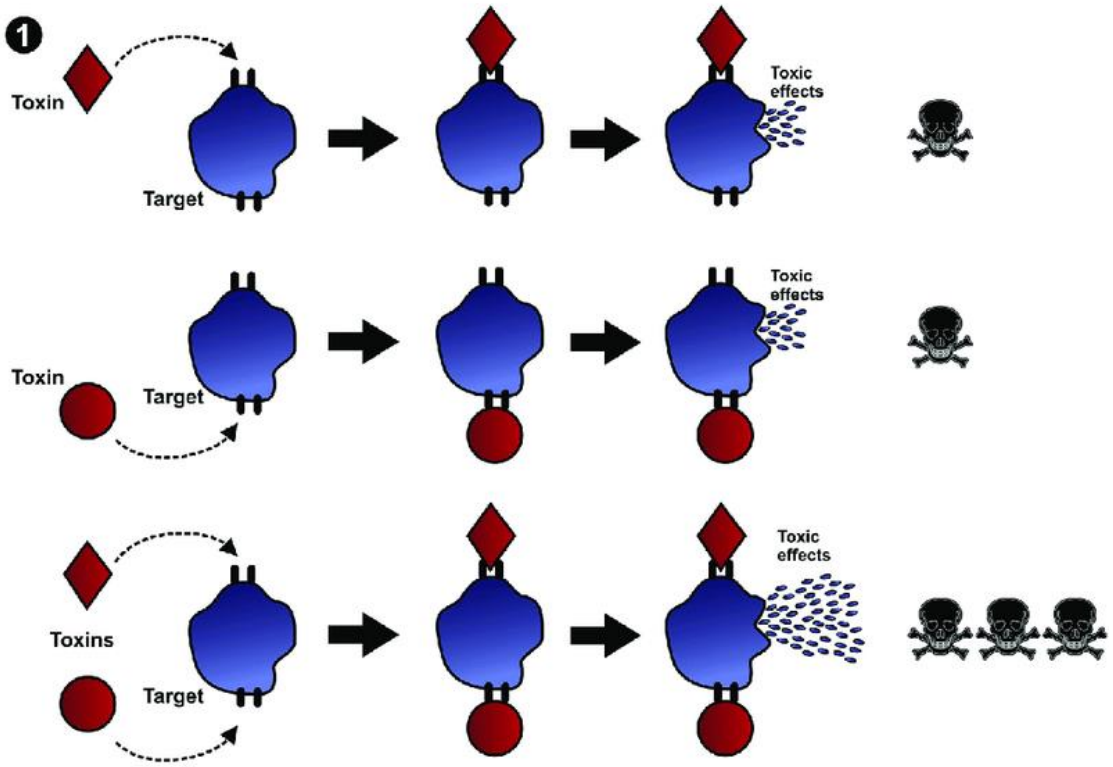
The precautionary principle

- The ***precautionary principle:***
  - Do not proceed with new actions, or at least proceed with extreme caution, until the ramifications of those new actions are well understood.
  - "Assume the worst, until proven otherwise."
- Regulatory agencies (EPA, FDA, CDC) apply the precautionary principle in determining safe exposure levels for toxic substances.
  - For each of the three levels of uncertainty described previously, the experimentally determined "safe" dosage concentration is divided by 10.
  - This results in the safe exposure dosages that are 1000x lower than determined for animals in animal studies.
  - This is thought to be a very conservative and cautious approach to determining safe exposure levels.

The Precautionary Principle

Combinations of substances in the environment create even greater uncertainty

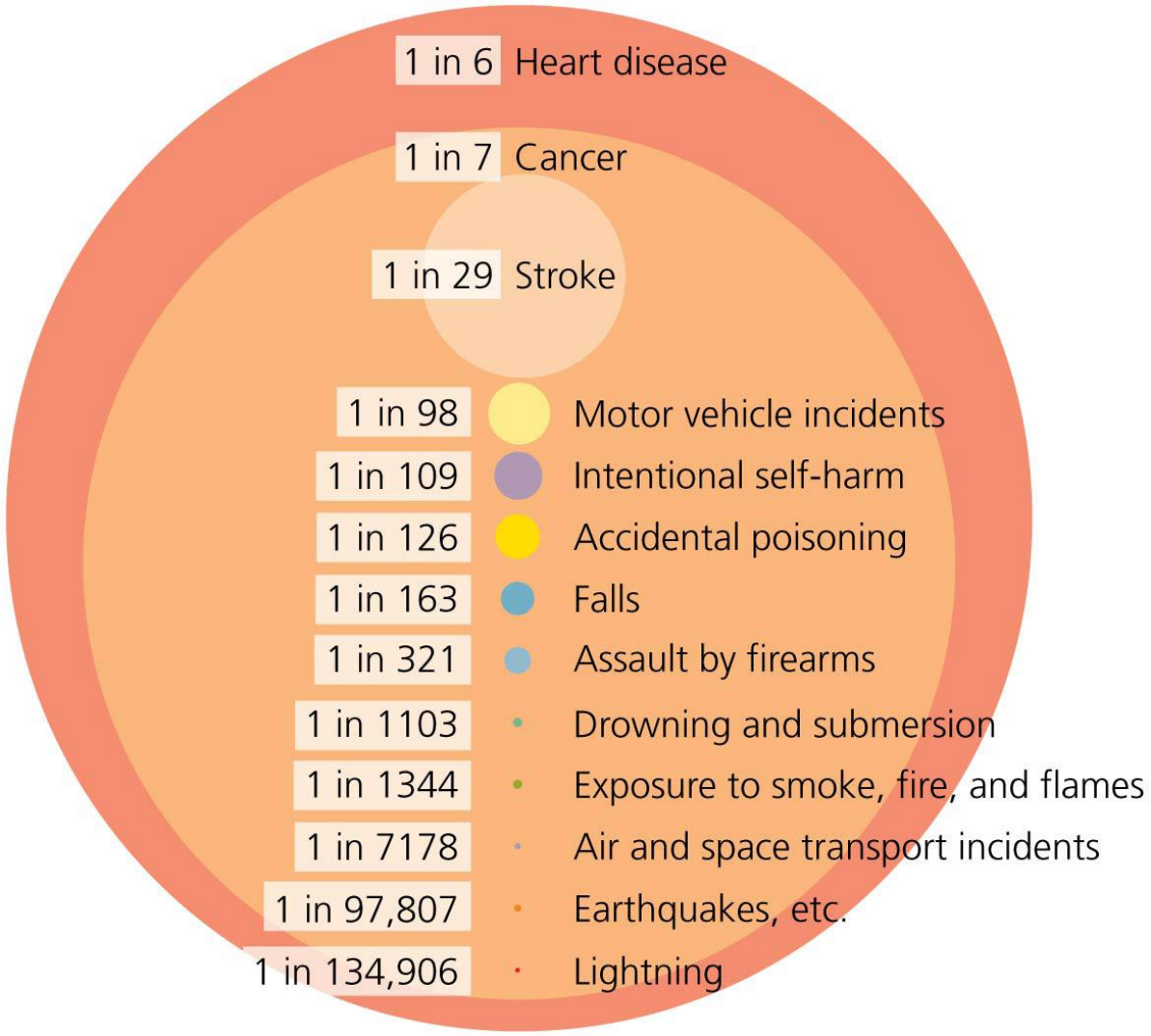
- The use of dose-response analysis in animal studies usually considers the effects of a single toxin tested over a range of doses, but chemical substances, when mixed together, may cause effects not predicted by each alone.
  - Mixed toxicants can sum, cancel out, or multiply each other's effects
  - ***Synergistic effects*** are interactive impacts that are greater than the sum of their constituent effects
    - Additive effect 2 + 2 = 4
    - **Synergistic effect 2 + 2 = 20**
    - Antagonistic effect: 2 + 2 = 1
    - Mice exposed to a mixture of nitrates, atrazine, and aldicarb (fertilizer, an herbicide and an insecticide) showed immune, hormone, and nervous system effects that were not evident when tested individually.



- The interactive effects of most chemicals are unknown.
  - This is slowly changing, but there are so many chemicals, and exponentially more combinations of these chemicals.

We assess risk in terms of probability

- Presence of health threats doesn't automatically produce an effect
  - Rather, it causes some probability (likelihood) of harm
- The threat a substance poses depends on its:
  - identity and strength
  - the chance and frequency of an encounter
  - and an organism's level of exposure and sensitivity to the threat
- ***Risk:*** the probability that some harmful outcome will result from a given action, event, or substance.
  - ***Perceived risks*** are often believed to be greater than the actual risk



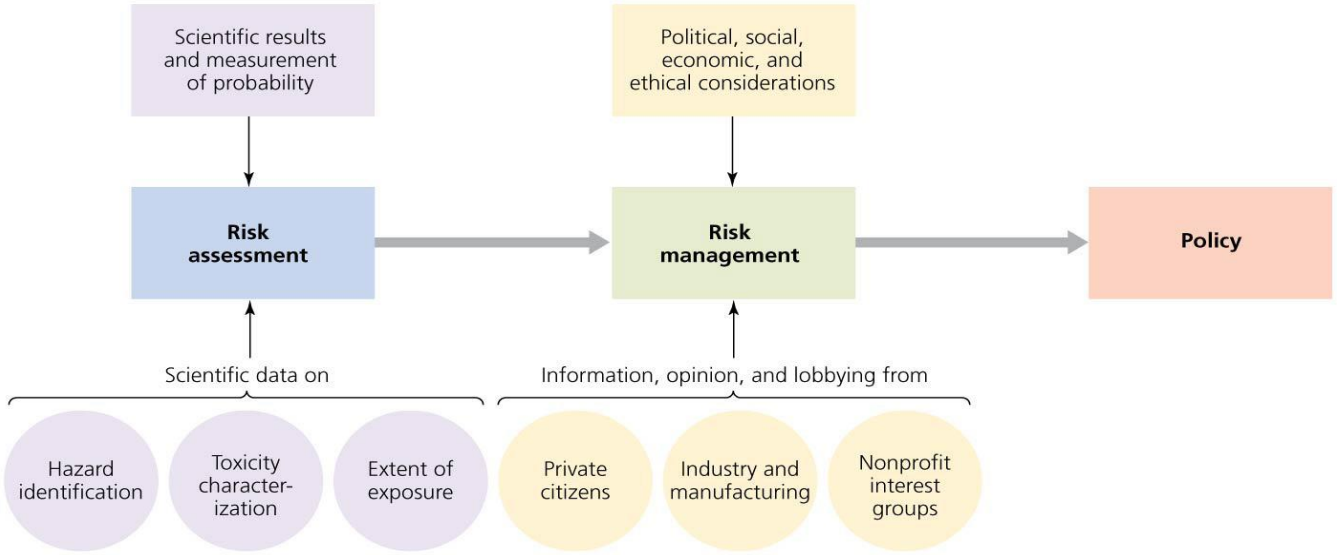
Risk assessment and risk management guide policy

Risk assessment has several steps. If assessing a chemical substance:

1. Identification of Hazard
2. Conduct a scientific study of toxicity (dose-response analysis)
3. Exposure Assessment: Assess an individual or population's exposure to the substance (frequency, intensity, duration)
4. Risk characterization: Teams of scientific experts review studies and determine the probability of harmful effects based on the *toxicity of the substance* and *the likelihood of exposure* to toxic doses.

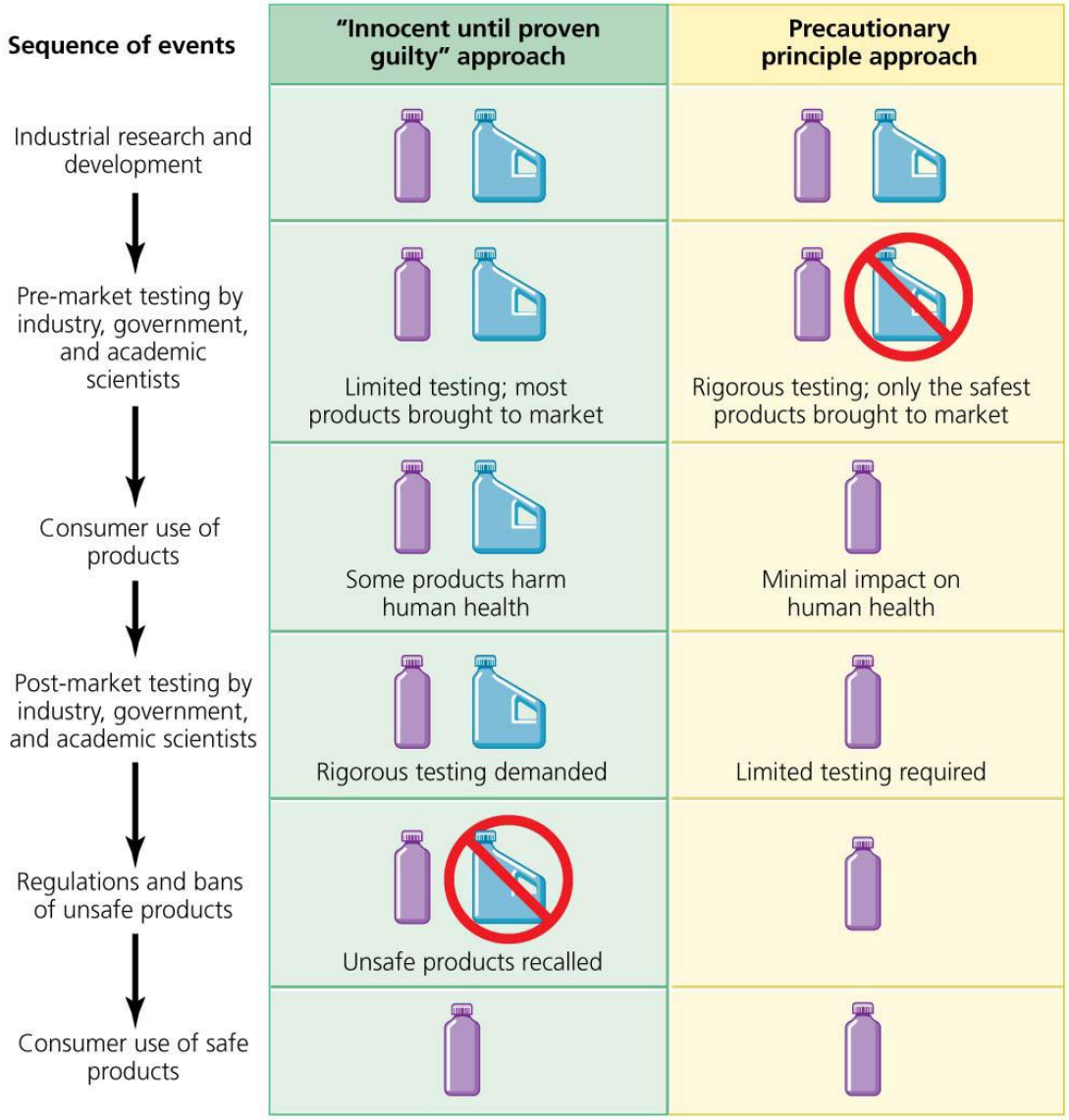
- Federal agencies manage risk
  - Centers for Disease Control and Prevention (CDC),
  - Environmental Protection Agency (EPA)
  - Food and Drug Administration (FDA)

- Scientific assessments are considered with economic, social, and political needs and values . Comparing costs and benefits is hard
  - Benefits are economic and easy to calculate
  - Health risk costs are hard-to-measure probabilities of a few people suffering a lot and lots of people not suffering at all.



Two approaches exist for determining safety

- Two philosophies exist for determining safety:
- The ***"innocent-until-proven-guilty"*** approach assumes a substance is harmless until shown to be harmful.
  - Helps technological innovation and economic advancement by limiting initial testing.
  - But allows dangerous substances to be widely used, before later determination of greater risk
  - The U.S. approach to chemical safety
- The ***precautionary principle approach*** assumes a substance is harmful until it is shown to be harmless.
  - Identifies troublesome toxicants before being released
  - May impede the pace of technology and economic advance due to a higher burden of proof.
  - The European approach to chemical safety



Toxic substance regulations

- The ***Toxic Substances Control Act (1976)*** directs the EPA to monitor (but not test) thousands of chemicals made in or imported into the United States
  - The EPA can ban substances that pose excessive risk
- Many health advocates think the TSCA is too weak.
  - 83,000 synthetic chemicals in use before 1976 were grandfathered into the approved list without further testing
  - To push for more testing, toxicity must already be demonstrated, but the EPA can not do testing to show toxicity unless proof of toxicity already exists.
- ***The Stockholm Convention*** on Persistent Organic Pollutants (POPs) was enacted in 2004 and ratified by over 150 nations
  - The Stockholm Convention sets guidelines for phasing out the "dirty dozen"
  - the 12 most dangerous POPs
  - Encouraging transition to safer alternatives.
- The ***Delaney Clause (1958) of the Food, Drug, and Cosmetics Act (1938)***
  - Bans the use of food additives found to induce cancer in humans or lab animals at any dosage.

TABLE 14.4 The "Dirty Dozen" Persistent Organic Pollutants (POPs) Targeted by the Stockholm Convention

TOXICANT	DESCRIPTION
Aldrin	Insecticide to kill termites and crop pests
Chlordane	Insecticide to kill termites and crop pests
DDT	Insecticide to protect against insect-spread disease; still applied in some countries to control malaria
Dieldrin	Insecticide to kill termites, textile pests, crop pests, and disease vectors
Dioxins	By-product of incomplete combustion and chemical manufacturing; released in metal recycling, pulp and paper bleaching, auto exhaust, tobacco smoke, and wood and coal smoke
Endrin	Pesticide to kill rodents and crop insects
Furans	By-product of processes that release dioxins; also present in commercial mixtures of PCBs
Heptachlor	Broad-spectrum insecticide
Hexachlorobenzene	Fungicide for crops; released by chemical manufacture and processes that release dioxins and furans
Mirex	Household insecticide; fire retardant in plastics, rubber, and electronics
PCBs	Industrial chemical used in heat-exchange fluids, electrical transformers and capacitors, paints, sealants, and plastics
Toxaphene	Insecticide to kill crop insects and livestock parasites

Data from United Nations Environment Programme (UNEP), 2001.

Video Resources

- Health Impacts of Pollutants
  - https://www.youtube.com/watch?v=VcDjyxanOyk