Risk Assessment

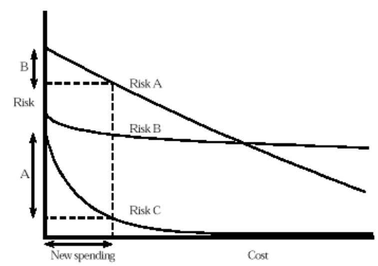
- The process of estimating both the **probability** that an event will occur and the probable **magnitude** of its adverse effects.
  - Based on Toxicology, Epidemiology, Economics, and Social Factors

Use Risk Assessment to …

- Target Prevention Measures
- Perform Remediation
- Allocate Resources (Risk Management)
- Alter procedures
- Develop controls

- Iterative process, not a one-time decision
- Must consider cumulative effects of all exposure (additive effect of multiple routes)
- Not all individuals have the same degree of risk to a given hazard
- Must balance likelihood of exposure with severity of consequences
  - Low frequency / Catastrophic event (Bhopal)
  - Low level exposure / Chronic heath problems

- Risk Management - regulatory process which considers social, political, engineering and **economic** issues.



Comparative Risk Assessment

- Risk is in everything we do ! Lifetime risk of death from all causes is 100%

- Must compare one risk with others to place it **in context**. This does not by itself establish the ***acceptability*** of the risk.

IN CLASS EXERCISE

- Rank the individual risk of anyone (not your personal risk, but generic risk) dying in a year from this activity/event/cause.
  - #1 Most risk
  - #30 Least risk

You have 20 minutes.

Perception of Risk

For this list of 20 items, assign a weight factor (1 - 9)

✓**Factor 1**

1 ……………… 9

- **controllable or uncontrollable**
- **voluntary or involuntary**
- **non-fatal or fatal**

✓**Factor 2**

1 ……………… 9

- **observable or unobservable**
- **immediate or delayed effect**
- **known or unknown**

Again you have 20 minutes.

Public Perception of Risk

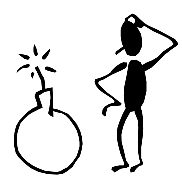
- *Voluntary risk is always more acceptable than involuntary risk !*
  - The same person who happily drives a car to work and back each day (about 1:100 lifetime odds of mortality) might be afraid of riding in a train (1:142,036) or horrified at the concept of drinking water containing the EPA limit of TCE (estimated to be 1:10,000,000).

Clark R. Chapman and David Morrison, "Impacts on the Earth by asteroids and comets: assessing the hazard", Nature, v. 367, pp. 33-39, **January 1994**.

Table 3 Chances of dying from selected causes (USA)

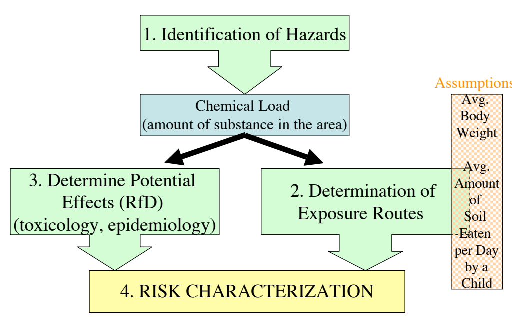
Cause	Chances
Motor vehicle accident	1 in 100
Murder	1 in 300
Fire	1 in 800
Firearms accident	1 in 2,500
Asteroid/comet impact (low limit)	1 in 3,000
Electrocution	1 in 5,000
Asteroid/comet impact	1 in 20,000
Passenger aircraft crash	1 in 20,000
Flood	1 in 30,000
Tornado	1 in 60,000
Venomous bite or sting	1 in 100,000
Asteroid/comet impact (high limit)	1 in 250,000
Fireworks accident	1 in 1 million
Food poisoning by botulism	1 in 3 million
Drinking water with EPA limit of TCE	1 in 10 million

- Regulatory reluctance to explicitly define "***acceptable***" risk - how much TCE do you think is acceptable in your water ?



- It is *"generally agreed"* that a lifetime risk on the order of **one in a million** (in the range of 10^{-6} - 10^{-5}) is small enough to be *acceptable* to the general public
  - Think about this - projected to 02/15/07 at 14:28 GMT (EST+5) there are 301,178,322 people in the U.S. - that is between 301 - 3,011 additional deaths over the average lifetime (~70 years) *per cause*
- For smaller exposed populations (workers at a chemical plant for example) a higher risk is may be considered tolerable (10^{-4})

Risk Assessment



1. Hazard Assessment

- Determine the nature of the hazard (in this case the toxin) and the extent of the harm.
  - Review of all relevant data on agent and the specific threat under investigation
    - Clinical studies of disease can identify large risks (1:10 or 1:100)
    - Epidemiological approaches detect risk down to 1:1,000 or for very large studies 1:10,000
    - The 1:1,000,000 limit is estimated by ***extrapolating*** the effects from Toxicological Studies

2. Exposure Assessment

- Measuring / Estimating the intensity, frequency, and duration of exposure via all logical potential pathways
- Nature, location and activity patterns of exposed or potentially exposed populations

2. Exposure Assessment

- ***Exposure Pathway*** - the course a hazard takes from sources to receptor - via vehicle or vector (i.e. air, water, insect …)
- ***Exposure Route*** - the method by which intake occurs (inhalation, injection, …)
- Monitoring and Modeling used to arrive at an ***Exposure Concentration*** (dose)

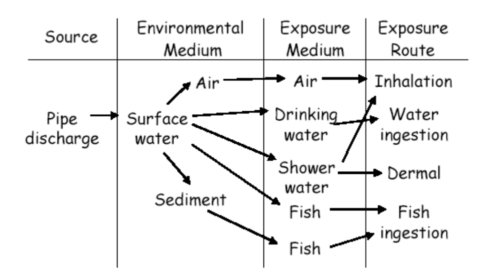
Behavior can vary wildly from person to person so …

Exposure Routes

EPA Standard Default Exposure Factors

Exposure Pathway	Daily Intake
Ingestion of potable water	2 L
Ingestion of soil and dust	200 mg (child) 100 mg (adult)
Inhalation of contaminants	20 m^3 (total - adult) residential
Consumption of homegrown produce	42 g fruit 80 g vegetable
Consumption of locally caught fish	54 g

Exposure to one toxin can occur via many different routes - Must examine cumulative result



Chemical Parameters
used to estimate distribution in the environment

- K_{ow} - octanol-water partition coefficient
- K_{oc} - organic carbon partition coefficient
- K_d - soil-water distribution coefficient
- BCF - bioconcentration factor
- H - Henry's Law constant

Rules of Thumb

low	(parameter)	high
	K_{ow}	soil
water	K_{oc}	sediment
	K_d	biota (fat)
	BCF	
water	H	air

Calculation of Absorbed Dose From Potential Dose:

$$\text{Potential Dose} = \frac{C \times IR \times ED}{AT \times BW}$$

Absorbed Dose = Potential Dose x AF

Where:
C = Contaminant Concentration IR = Intake Rate
ED = Exposure Duration AT = Averaging Time
BW = Body Weight
AF = Fraction of Potential Dose Absorbed

Calculate the lifetime average daily potential dose of PCBs that a person would get from a daily average intake of 30 g of fish containing 2.5 mg/kg of PCBs for 30 years.

- Express potential dose in units of mg/kg-day (concern is cancer risk).

Answer

Potential Dose =

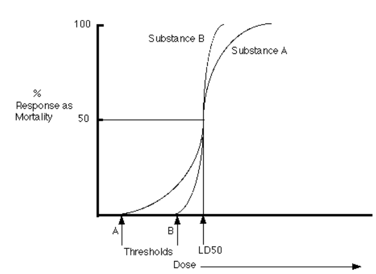
$$\frac{2.5\ \text{mg/kg} \times 30\ \text{g/day} \times 365\ \text{days/yr} \times 30\ \text{yrs} \times 10^{-3}\ \text{kg/g}}{70\ \text{kg} \times 70\ \text{yrs} \times 365\ \text{days/yr}}$$

$= 5 \times 10^{-4}$ mg/kg-day

3. Potential Effects

- Examination of toxicology and epidemiology reports
- Goal is to establish a **mathematical relationship** between amount of hazard/toxin and the risk of adverse outcomes from a specific dose.

Acute Toxicity -
LD_{50} does not tell the whole story



- Most data available is from high dosage animal studies conducted over a short period of time - this needs to be converted into low dosage long term human
- Many mathematical models exist for this conversion - choice of model is a *policy* decision.

RfD

- One approach used for toxins that have thresholds is the *Reference Dose* (RfD)
  – The dose of toxin per unit body weight per day (mg kg^{-1} day^{-1}) that is likely to pose no appreciable risk to human populations, including sensitive individuals.

$$RfD = \frac{NOAEL}{SF_1 \times SF_2 \times \ldots}$$

(Organizations other than the EPA call this the **ADI** or acceptable daily intake)

RfD

1. Select the most sensitive/applicable species for which adequate studies are available (human data is always given priority)
2. Establish exposure route (RfDs are route specific)
3. Gather supporting studies/information
4. Identify the NOAEL, or if such data is not available, the LOAEL for the most sensitive endpoint

RfD

5. Apply Safety Factors

Adjust by

- ÷ 10 to include most sensitive populations (children, elderly …)
- ÷ 10 when extrapolating from animals to humans
- ÷ 10 when using sub-chronic instead of chronic study data
- ÷ 10 when using a LOAEL instead of a NOAEL

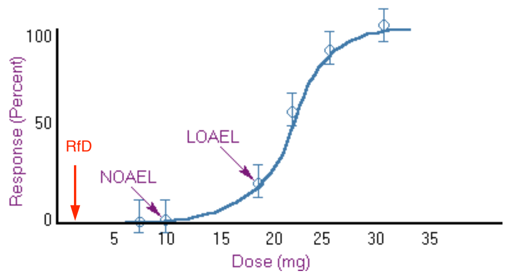
Example …

- In a subchronic oral toxicity study in mice, a lowest observed adverse effect level (LOAEL) of 5mg/kg•day was determined for a specific agent. The quality of the data is rated as high. What is the RfD ?

- Solution

Area of uncertainty	Safety Factor
Variation in population	10
Extrapolation from animal to human	10
Extrapolation from subchronic to chronic	10
Extrapolation from LOAEL to NOAEL	10
Quality of data	1

RfD = (5mg/kg•day) / (10x10x10x10x1)
= 0.5µg /kg•day



Using RfDs

Calculation of non-carcinogenic risk

Hazard Quotant (HQ) for a single substance

Hazard Index (HI) for multiple substances

$$HQ = \frac{\text{Average daily dose (mg/kg•day)}}{\text{RfD (mg/kg•day)}}$$

HI = HQ + HQ + HQ … + HQ

HI/HQ less than 1.0 is "not unacceptable"

Use of RfDs

- Water contaminated by a nearby metal plating facility was shown to contain cyanide at 0.03 mg/L, nickel at 0.12 mg/L, and chromium(III) at 12.4 mg/L. If the daily water intake is assumed to be 2L and the average body weight of an adult human is 70 kg, do these exposures indicate an unacceptable hazard ?

RfDs

- Cyanide 0.02 mg/kg•day
- Nickel 0.02 mg/kg•day
- Chromium(III) 1.0 mg/kg•day

Solution

	C (mg/L)	Dose (mg/kg•day)	Hazard Ratio (dose/RfD)
Cyanide	0.03	8.57×10^{-4}	0.04
Nickel	0.12	3.43×10^{-3}	0.17
Chromium	12.4	0.35	0.35
			0.56

0.56 is less than 1.0, therefore this is "not unacceptable"

Chronic Daily Intake (CDI)

- The average exposure/dose over a lifetime normalized to daily amounts

$$CDI = \frac{\text{(concentration) x (intake rate) x (days of exposure/lifetime)}}{\text{(lifetime)}}$$

$$CDI\ (\text{mg/kg•day}) = \frac{\text{"Average daily dose (mg/kg)"}}{\text{Body weight (kg)}}$$

CDI

- Chronic Daily Intake and RfD can be used to estimate **non-cancer** risk as follows

RISK = PF (CDI - RfD)

PF = potency factor - slope of dose response curve also called slope factor (SF)
(see www.epa.gov/iris)

Example

- Calculate CDI for a person eating locally caught fish from waters containing 100ppb (0.1 mg/L) TCE; bioconcentration TCE in fish = 1.06 mg TCE per kg fish. Fish is only exposure.

Std. Exp = 70kg person eats 54 g of fish for 350 days/yr for 30 years

Total intake

CDI =

$$\frac{(.054 \text{ kg fish})\text{x}(1.06 \text{ mg TCE/kg fish})\text{x}(350 \text{ days/yr})\text{x}(30 \text{ years})}{70 \text{ kg x } 70 \text{ year lifespan x } 365 \text{ days/yr}}$$

Spread over lifetime

CDI = 3.36×10^{-4} (mg/kg•day)

RISK =
PF ($3.36\text{x}10^{-4}$ mg/kg•day - $1.00\text{x}10^{-4}$ mg/kg•day)

PF = $1.1\text{x}10^{-2}$ kg •day /mg

Risk = $1.1\text{x}10^{-2}$ kg•day /mg x ($2.36\text{x}10^{-4}$ mg/kg•day)
RISK = $2.6\text{x}10^{-6}$ or 2.6 in a million

This calculation is actually pretty rare - usually
For non-cancerous contaminants the risk is assumed zero if the CDI ≤ RfD.

Cancer Risks

Group	Category
A	Human carcinogen
B	Probable human carcinogen: B1 indicates limited human evidence; B2 indicates sufficient evidence in animals and inadequate or no evidence in humans
C	Possible human carcinogen
D	Not classifiable as to human carcinogenicity
E	Evidence of noncarcinogenicity for humans

Using CDI to calculate **cancer** risk

Incremental lifetime cancer risk based on certain exposure:

RISK = (PF x CDI)

Assuming a <u>linear</u> dose-response relationship

Example

- If our fish also contained 1.06 mg of Aniline, what would the cancer risk be ?

Std. Exp = 70kg person eats 54 g of fish for 350 days/yr for 30 years

CDI =

$$\frac{(.054 \text{ kg fish})\text{x}(1.06 \text{ mg Aniline/kg fish})\text{x}(350 \text{ days/yr})\text{x}(30 \text{ yr})}{70 \text{ kg x } 70 \text{ year lifespan x } 365 \text{ days/yr}}$$

CDI is still = 3.36×10^{-4} (mg/kg•day)

Example

CDI = 3.36×10^{-4} (mg/kg•day)
PF = 5.7×10^{-3} (kg •day/mg)

RISK = PF x CDI

Risk = 3.36×10^{-4}(mg/kg•day) x 5.7×10^{-3}(kg •day/mg)
Risk = 1.9×10^{-6} or 1.9 in a million

Risk Communication

"'Be Careful'! All you can tell me is 'Be careful'?"