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 health 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).

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


Table 3 Chances of dying from selected causes (USA)

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

- It is "generally agreed" that a lifetime risk on the order of one in a million (in the range of $10^{-6}$ - $10^{-3}$) 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 ($10^{-3}$)

### Risk Assessment

1. Identification of Hazards
2. Determination of Exposure Routes
3. Determine Potential Effects (RID) (toxicology, epidemiology)
4. RISK CHARACTERIZATION

Assumptions

- Body Weight
- Avg. Amount of Soil Eaten per Day by a Child
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)

---

### Chemical Parameters

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

---

### Exposure Routes

<table>
<thead>
<tr>
<th>Exposure Pathway</th>
<th>Daily Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingestion of potable water</td>
<td>2 L</td>
</tr>
</tbody>
</table>
| Ingestion of soil and dust | 200 mg (child)
| Inhalation of contaminants | 100 mg (adult) |
| Consumption of homegrown produce | 20 m³ (total - adult) residential |
| Consumption of locally caught fish | 42 g fruit
| | 80 g vegetable |
| | 54 g         |
**Rules of Thumb**

<table>
<thead>
<tr>
<th>low (parameter)</th>
<th>high (parameter)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K_{sw}$</td>
<td>soil</td>
</tr>
<tr>
<td>$K_{sc}$</td>
<td>sediment</td>
</tr>
<tr>
<td>$K_d$</td>
<td>biota (fat)</td>
</tr>
<tr>
<td>BCF</td>
<td></td>
</tr>
<tr>
<td>water</td>
<td>H</td>
</tr>
<tr>
<td></td>
<td>air</td>
</tr>
</tbody>
</table>

**Calculation of Absorbed Dose From Potential Dose:**

Potential Dose = \[ \frac{C \times IR \times ED}{AT \times BW} \]

Absorbed Dose = Potential Dose \times AF

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

**Answer**

Potential Dose = 
\[ \frac{2.5 \text{ mg/kg} \times 30 \text{ g/day} \times 365 \text{ days/yr} \times 30 \text{ yrs} \times 10^{-3} \text{ kg/g}}{70 \text{ kg} \times 70 \text{ yrs} \times 365 \text{ days/yr}} \]

\[ = 5 \times 10^{-4} \text{ mg/kg-day} \]

**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 studies.

• 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

5. Apply Safety Factors

<table>
<thead>
<tr>
<th>Area of uncertainty</th>
<th>Safety Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variation in population</td>
<td>10</td>
</tr>
<tr>
<td>Extrapolation from animal to human</td>
<td>10</td>
</tr>
<tr>
<td>Extrapolation from subchronic to chronic</td>
<td>10</td>
</tr>
<tr>
<td>Extrapolation from LOAEL to NOAEL</td>
<td>10</td>
</tr>
<tr>
<td>Quality of data</td>
<td>1</td>
</tr>
</tbody>
</table>

\[
RfD = \frac{5 \text{mg/kg-day}}{(10 \times 10 \times 10 \times 10)} = 0.5 \text{mg/kg-day}
\]

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 ?
Using RfDs
Calculation of non-carcinogenic risk

**Hazard Quotant (HQ)** for a single substance

**Hazard Index (HI)** for multiple substances

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

$$ HI = HQ + HQ + HQ \ldots + HQ $$

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\cdot day
- Nickel: 0.02 mg/kg\cdot day
- Chromium(III): 1.0 mg/kg\cdot day

Solution

<table>
<thead>
<tr>
<th></th>
<th>C (mg/L)</th>
<th>Dose (mg/kg\cdot day)</th>
<th>Hazard Ratio (dose/RfD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyanide</td>
<td>0.03</td>
<td>8.57x10^{-4}</td>
<td>0.04</td>
</tr>
<tr>
<td>Nickel</td>
<td>0.12</td>
<td>3.43x10^{-3}</td>
<td>0.17</td>
</tr>
<tr>
<td>Chromium(III)</td>
<td>12.4</td>
<td>0.35</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.35</td>
<td>0.56</td>
</tr>
</tbody>
</table>

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

$$ CDI = (\text{concentration} \times \text{intake rate} \times \text{days of exposure/lifetime}) / \text{body weight (kg)} $$

$$ CDI (\text{mg/kg\cdot day}) = \frac{\text{“Average daily dose (mg/kg)”}}{\text{Body weight (kg)}} $$
CDI

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

\[ \text{RISK} = \text{PF} \times (\text{CDI} - \text{RfD}) \]

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.

\[ \text{Std. Exp} = 70\text{kg person eats 54 g of fish for 350 days/yr for 30 years} \]

\[ \text{CDI} = \frac{(0.054 \text{ kg fish}) \times (1.06 \text{ mg TCE/kg fish}) \times (350 \text{ days/yr}) \times (30 \text{ years})}{70 \text{ kg x 70 year lifespan x 365 days/yr}} \]

Total intake

Spread over lifetime

\[ \text{CDI} = 3.36 \times 10^{-4} \text{(mg/kg•day)} \]

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

PF = 1.1 \times 10^{-2} \text{ kg•day/mg}

Risk = 1.1 \times 10^{-2} \text{ kg•day/mg} \times (2.36 \times 10^{-4} \text{ mg/kg•day})

\[ \text{RISK} = 2.6 \times 10^{-6} \text{ or 2.6 in a million} \]

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

Using CDI to calculate cancer risk

Incremental lifetime cancer risk based on certain exposure:

\[ \text{RISK} = \text{(PF x CDI)} \]

Assuming a linear dose-response relationship

Cancer Risks

<table>
<thead>
<tr>
<th>Group</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Human carcinogen</td>
</tr>
<tr>
<td>B</td>
<td>Probable human carcinogen</td>
</tr>
<tr>
<td>C</td>
<td>Likely human carcinogen</td>
</tr>
<tr>
<td>D</td>
<td>Not classifiable as to human carcinogenicity</td>
</tr>
<tr>
<td>E</td>
<td>Evidence of noncarcinogenicity for humans</td>
</tr>
</tbody>
</table>

Example

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

\[ \text{Std. Exp} = 70\text{kg person eats 54 g of fish for 350 days/yr for 30 years} \]

\[ \text{CDI} = \frac{(0.054 \text{ kg fish}) \times (1.06 \text{ mg Aniline/kg fish}) \times (350 \text{ days/yr}) \times (30 \text{ yr})}{70 \text{ kg x 70 year lifespan x 365 days/yr}} \]

\[ \text{CDI is still} = 3.36 \times 10^{-4} \text{(mg/kg•day)} \]
Example
CDI = 3.36 \times 10^{-4} \text{ (mg/kg\cdot day)}
PF = 5.7 \times 10^{-3} \text{ (kg \cdot day/mg)}

\text{RISK} = \text{PF} \times \text{CDI}

\text{Risk} = 3.36 \times 10^{-4} \text{ (mg/kg\cdot day)} \times 5.7 \times 10^{-3} \text{ (kg \cdot day/mg)}
\text{Risk} = 1.9 \times 10^{-6} \text{ or 1.9 in a million}

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