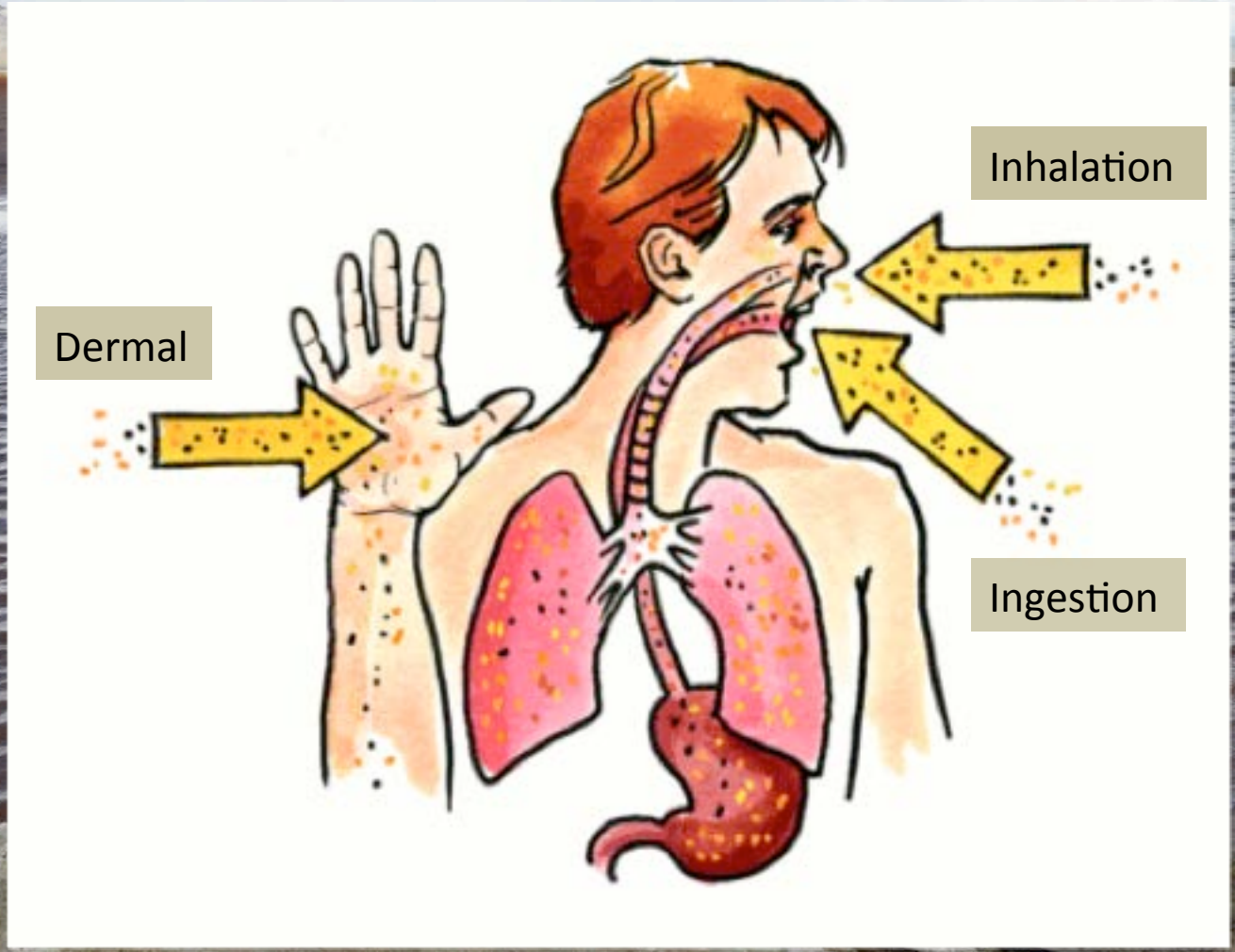
Human Toxicological Risk Assessment Principles

Documents used:
Phase 1A Attachment 10B Site Photographs

Outline

- Toxicity
- Non-Carcinogenic Hazard
- Carcinogenic Risk
- Site Specific Risk

Toxicity – Exposure Route

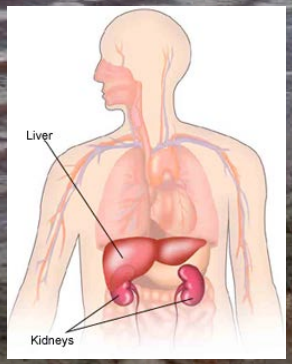


Toxicity – Target Organs

- **Inhalation**
  - Lungs: most detrimental effects
- **Ingestion**
  - Gastrointestinal Tract
  - Liver
  - Kidneys
- **Dermal**
  - Skin
  - Vascular system

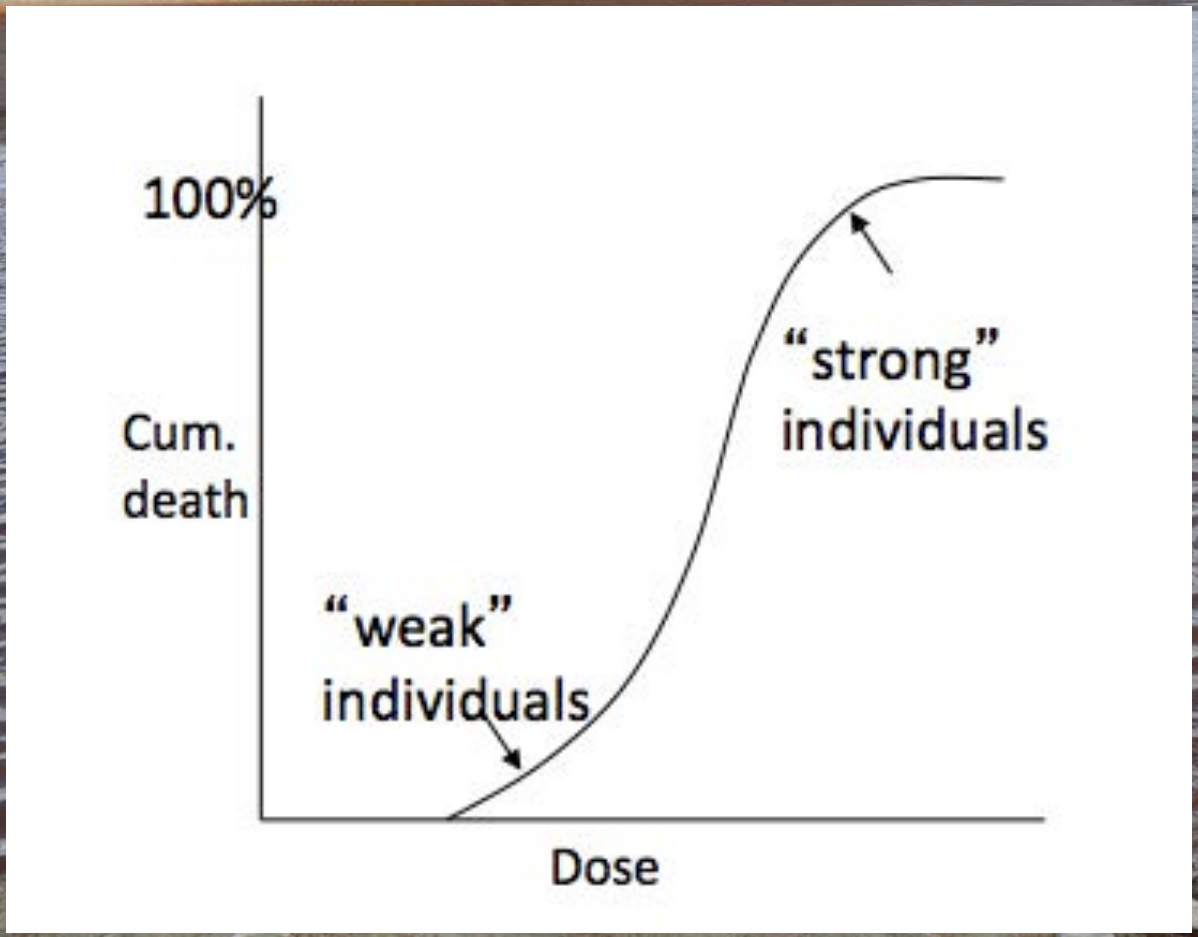
Toxicity – Fate

- **hydrophobic compounds**: end up in fatty tissues
- **Inorganic ions:** end up in bone (such as lead, radium, and fluoride)
- **heavy metals**: end up in the kidney and liver



Toxicity - Dose

“everything is a poison given a sufficient dose”

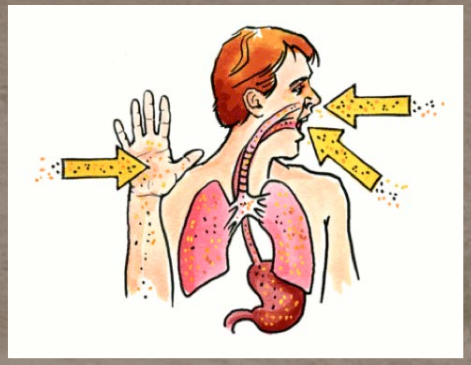


For a given dose, there will be a range of responses based on variability in the population in:

- Age
- Sex
- Diet
- Overall- health
- Genetics

Non-carcinogenic Hazard

- Reference Dose (R_fD):
  - Based on **LOAEL** (lowest observable adverse effects level) or **NOAEL** (no observable adverse effects level) from dose-response relationships



  - Dose-response data is taken from animal studies with species as close to human as possible

Non-carcinogenic Hazard

- Reference Dose (R_fD):
  - reduced by **safety factors** (1/10) to account for the following:
    - 1/10 for non-human subjects
    - 1/10 for sub-chronic versus chronic study
    - 1/10 for LOAEL versus NOAEL

Non-carcinogenic Hazard

- What is a safe Reference Dose (R_fD)?
- Hazard = Intake/ R_fD
  - –A safe number for non-carcinogenic effects is <1.0

Concentration | Contact Rate | Exposure Frequency | Exposure Duration

$$\text{Intake} = I = \frac{(C)(CR)(EF)(ED)}{(BW)(AT)} = \frac{mg_{compound}}{kg_{body\ weight}day}$$

Body Weight | Averaging Time

Non-Carcinogenic Hazard Example

- Suppose Jimmy eats a bowl of rice 4 times per week that contains 50 ng of arsenic per bowl for 40 years. Is his intake safe?

$$R_fD = 3.0E-4\,\frac{mg}{kg*day}$$

$$Hazard = \frac{\left(1.5\,\frac{kg*day}{mg}\right)}{3.0E-4\,\frac{mg}{kg*day}} = 2.73$$

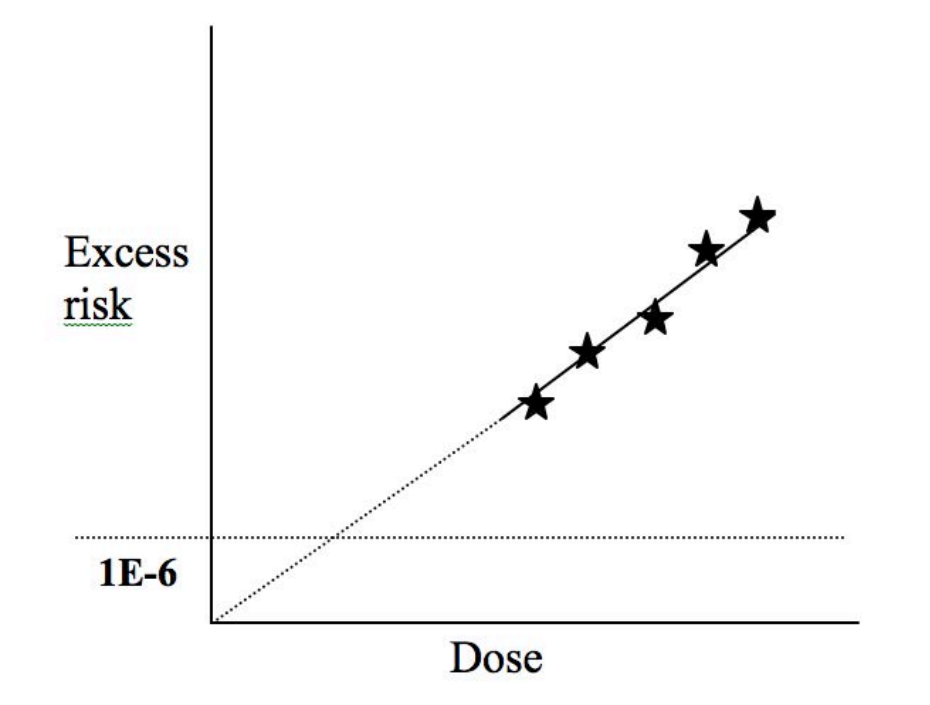
- Yes, because the hazard is greater than 1.0

http://cfpub.epa.gov/ncea/iris/compare.cfm

Excess Carcinogenic Risk

$$\text{Excess carcinogenic risk} = (I)(SF) = \frac{mg}{kg - day} \frac{excess\ risk}{\frac{mg}{kg - day}}$$

Slope Factor



Excess Carcinogenic Risk Example

- Suppose Jimmy eats a bowl of rice 4 times per week that contains 50 ng of arsenic per bowl for 40 years. What is his excess risk of developing cancer?

$$slope\ factor = 1.5\frac{kg * day}{mg}$$

$$Intake = \frac{100\frac{\mu g}{day}\frac{mg}{1000\mu g} * \frac{209\ days}{year}40\ years}{70\ kg * \frac{365 days}{year} * 40\ years} = 8.18E-4\frac{mg}{kg * day}$$

$$Excess\ Risk = \left(1.5\frac{kg * day}{mg}\right) * \left(8.18E-4\frac{mg}{kg * day}\right) = 1.23E-3$$

- Because this risk is greater than 1E-6 (1 in 1 million cancer background level) this is a high risk.

http://cfpub.epa.gov/ncea/iris/compare.cfm

Human Toxicology: Comparative Risk

Table 2
Some Commonplace Risks
(mean values with uncertainty)

Action	Lifetime Risk	Uncertainty
Motor vehicle accident (total)	1.7×10^{-2}	10≈
Motor vehicle accident (pedestrian only)	2.9×10^{-3}	10≈
Home accidents	7.7×10^{-3}	5≈
Electrocution	3.7×10^{-4}	5≈
Air pollution, eastern United States	1.4×10^{-2}	Factor of 00 downward only
Cigarette smoking, one pack per day	2.5×10^{-1}	Factor of 3
Sea-level background radiation (except radon)	1.4×10^{-3}	Factor of 3
All cancers	2×10^{-1}	10≈
Four tablespoons peanut butter per day	6×10^{-4}	Factor of 3
Drinking water with EPA limit of chloroform	4×10^{-5}	Factor of 10
Drinking water with EPA limit of trichloroethylene	1×10^{-7}	Factor of 10
Alcohol, light drinker	1×10^{-3}	Factor of 10
Police killed in line of duty (total)	1.5×10^{-2}	20≈
Police killed in line of duty (by felons)	9.1×10^{-3}	10≈
Frequent flying professor	4×10^{-3}	50≈
Mountaineering (mountaineers)	4×10^{-2}	50≈

Source: Based on annual risks presented by Wilson and Crouch, *Science*, April 17, 1987.

Comparative Carcinogenic Risk

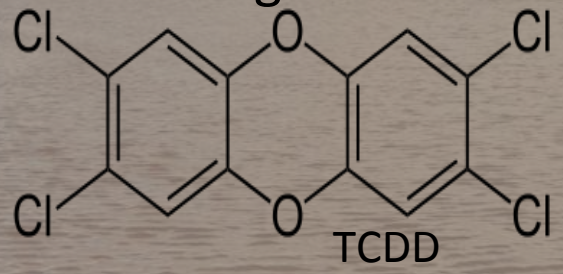
RISKS WHICH PRODUCE A PROBABILITY OF DEATH OF 0.000001 (1 DEATH IN 1 MILLION)

3	Cigarettes	Cancer, heart disease
2 months	Of living with a cigarette smoker	Cancer, heart disease
0.5 liter	Wine	Cirrhosis of the liver
40 tablespoons	Peanut butter	Liver and other cancer caused by aflatoxin
30 cans	Diet soda	Cancer caused by saccharin
2 months	In stone or brick building	Cancer caused by radioactivity
6,000 miles	Jet flying	Cancer caused by cosmic rays
2 months	Visit to Denver	Cancer caused by cosmic rays
2 days	In NY or Boston	Air pollution
1/12	Yearly diagnostic X-ray dose	Cancer

Toxins at the Site

Dioxins:

- Toxic dioxins among most potent human carcinogens
- Non-cancer risks:
  - Strong correlation with diabetes
  - Immunotoxicity



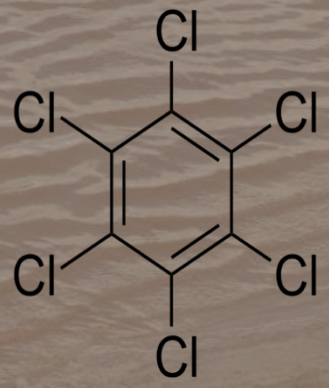
TCDD

Hexachlorobenzene (HCB):

- Bioaccumulates in fatty tissue (takes 15 years to rid HCB from the body)
- Probable human carcinogen

Non-cancer risks:

- Linked to diabetes
- Immunotoxicity (can lead to cancer)
- Liver damage
- Miscarriage/infant death



Toxins at the Site

Contaminant	Maximum Concentration	Location	Media
Dioxin (TEQ)	1.1 ppm	Central Ditch	Soil
Dioxin (TEQ)	2.41E-6 ppm	Monitoring Well 8A	Groundwater
HCB	2100 ppm	Central Ditch	Soil
HCB	2.8 ppb	Monitoring Well 8A	Groundwater
PCB	75.02 ppm	Main Ditch	Soil
PCB	NA	NA	Groundwater

Human Toxicology: Carcinogenic & Non-Carcinogenic

Waste Management Unit	**Estimated Cancer Risk**
Central Ditch	8 in 1,000
Western Ditch	3 in 1,000
Chlorine Ditch	2 in 1,000
Main Ditch	2 in 1,000
Old Waste Pond-Inlet Area	5 in 10,000
400 Acre Waste Pond	4 in 10,000
Courtyard	2 in 10,000
Old Waste Pond-Area Away from Inlet	1 in 10,000
Gypsum Pile	9 in 100,000
Boron Ditch	9 in 1,000,000
Smut Pile	1 in 1,000,000
Barium Sulfate Area	2 in 10,000,000

Any risk above 1 in 1 million is considered elevated and unsafe

Degrandchamp Expert Report 2007

Human Toxicology: Carcinogenic & Non-Carcinogenic

Contaminant	Average Body Burden	Maximum Body Burden (ppt)	Average Carcinogenic Risk	Maximum Carcinogenic Risk	Average Non-Carcinogenic Hazard
HCB*	3.4 ppb	19.0 ppb	NA	2 in 10,000	2.7 X safe levels
Dioxin**	41.5 ppt	175.9 ppt	8.2 in 1000	2.5 in 100	5 X safe levels

*Degrandchamp Expert Report, 2007
**Degrandchamp Expert Rebuttal Report 2007