風險評估與管理

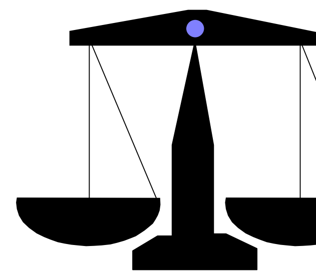
- Risk principles
- Steps in risk assessment
- Risk calculation
- Toxicology

What is Risk Assessment?

- “Risk Assessment is the process of determining, either **quantitatively or qualitatively**, the probability and magnitude of an undesired event.” (Oklahoma Corporation Commission Risk Assessment Guidance Document, 1994)

評估是科學的; 管理是政治的

- “Risk analysis … includes decisions which should be guided by social, cultural, moral, economic, and political factors …” (quoted in OCC RA Guidance Document)



- Decisions based on professional experience and judgment are valid.

Introduction

- 單位: $X/10^6$ (風險沒有單位)
- 種類: lifetime risk (70年); Annual risk
- 目的: 取得可接受風險與控制成本間平衡的起始點
- 感受性: 非理性/主觀

TABLE 4.2 Annual risks of death associated with certain activities.

Activity/exposure	Annual risk (Deaths per 100,000 persons at risk)
Motorcycling	2000
Smoking, all causes	300
Smoking (cancer)	120
Hang gliding	80
Coal mining	63
Farming	36
Motor vehicles	24
Chlorinated drinking water (chloroform)	0.8
4 tbsp peanut butter per day (aflatoxin)	0.8
3 oz charcoal broiled steak per day (PAHs)	0.5
1-in-a-million lifetime risk	0.0014

Source: Based on Wilson and Crouch, 1987.

death rate

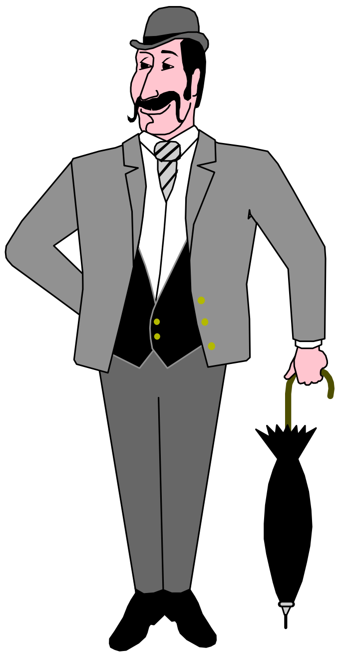
TABLE 4.3 Activities that increase mortality risk by one in a million

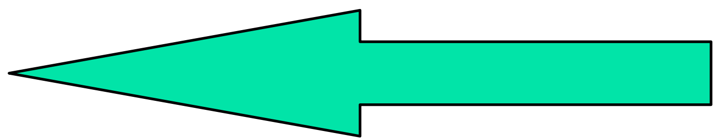
Activity	Type of risk
Smoking 1.4 cigarettes	Cancer, heart disease
Drinking 1/2 liter of wine	Cirrhosis of the liver
Spending 1 hour in a coal mine	Black lung disease
Living 2 days in New York or Boston	Air pollution
Traveling 300 miles by car	Accident
Flying 1000 miles by jet	Accident
Flying 6000 miles by jet	Cancer by cosmic radiation
Traveling 10 miles by bicycle	Accident
Traveling 6 minutes by canoe	Accident
Living 2 summer months in Denver (vs. sea level)	Cancer by cosmic radiation
Living 2 months with a cigarette smoker	Cancer, heart disease
Eating 40 tablespoons of peanut butter	Liver cancer caused by aflatoxin
Eating 100 charcoal-broiled steaks	Cancer from benzopyrene
Living 50 years within 5 miles of a nuclear reactor	Accident releasing radiation

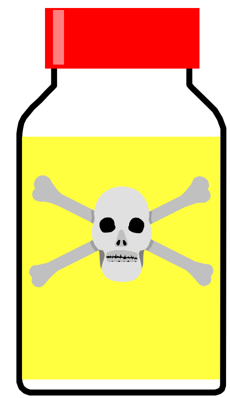
Source: Wilson (1979).

- Risk = Exposure x Toxicity

Receptor---- Pathways ----Source





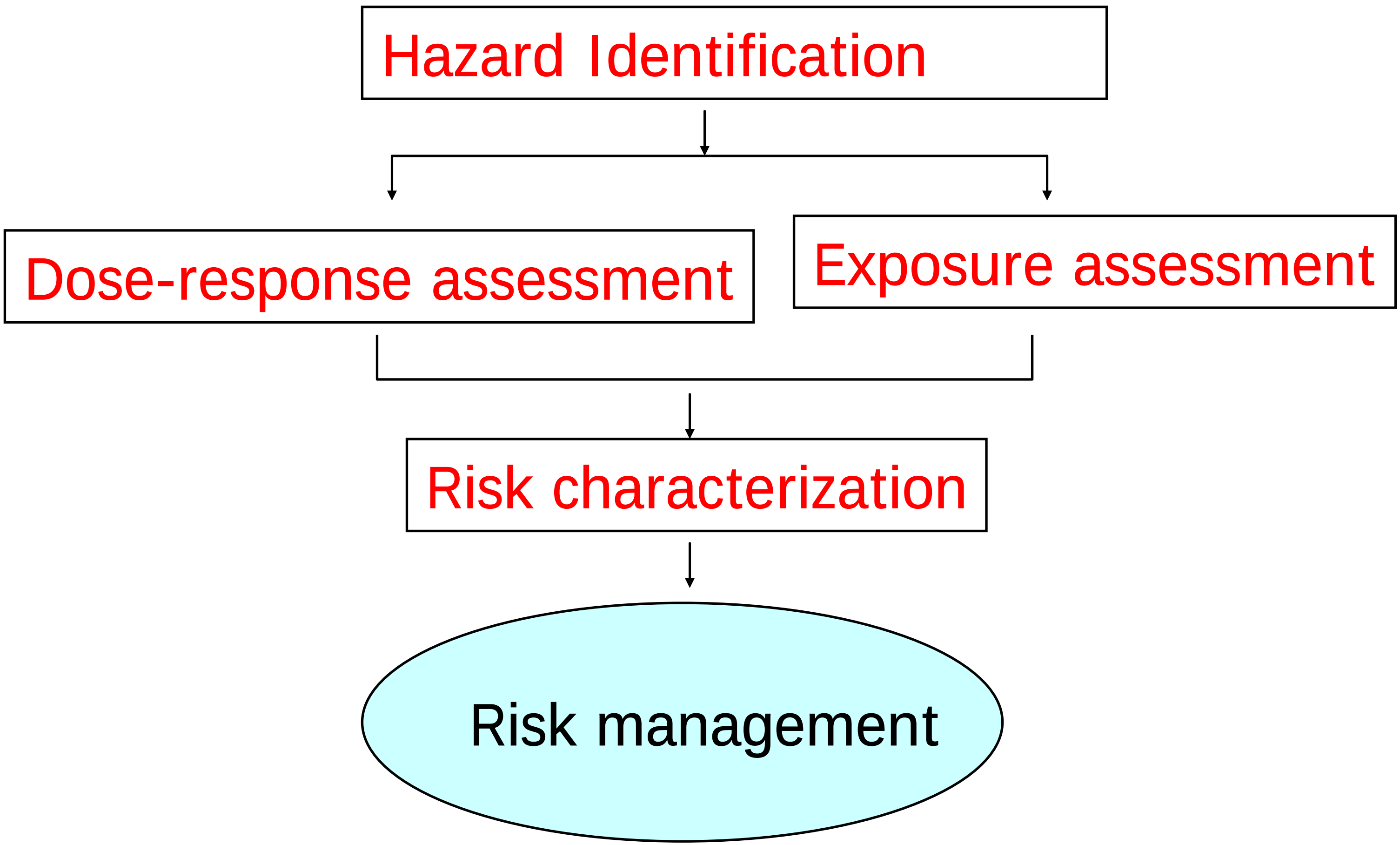


Nanomaterials?

Steps in Risk Assessment

- **STEP 1**: Look for the hazards (Hazard Identification)
- **STEP 2**: Decide who might be harmed and how (Exposure assessment and Dose-response)
- **STEP 3**: Evaluate the risks and decide whether the existing precautions are adequate or whether more should be done (Risk characterization)
- **STEP 4**: Record your findings
- **STEP 5**: Review your assessment and revise it if necessary

風險評估的程序


Hazard Identification
Dose-response assessment
Exposure assessment
Risk characterization
Risk management

Hazard Identification

- Chemicals of concern
- Description of Chemicals
- Reason for concern

Hazard and Risk
Hazard Anything that can cause harm (e.g., chemicals, electricity, working from ladders, etc.).
Risk The chance, high or low, that somebody will be harmed by the hazard.

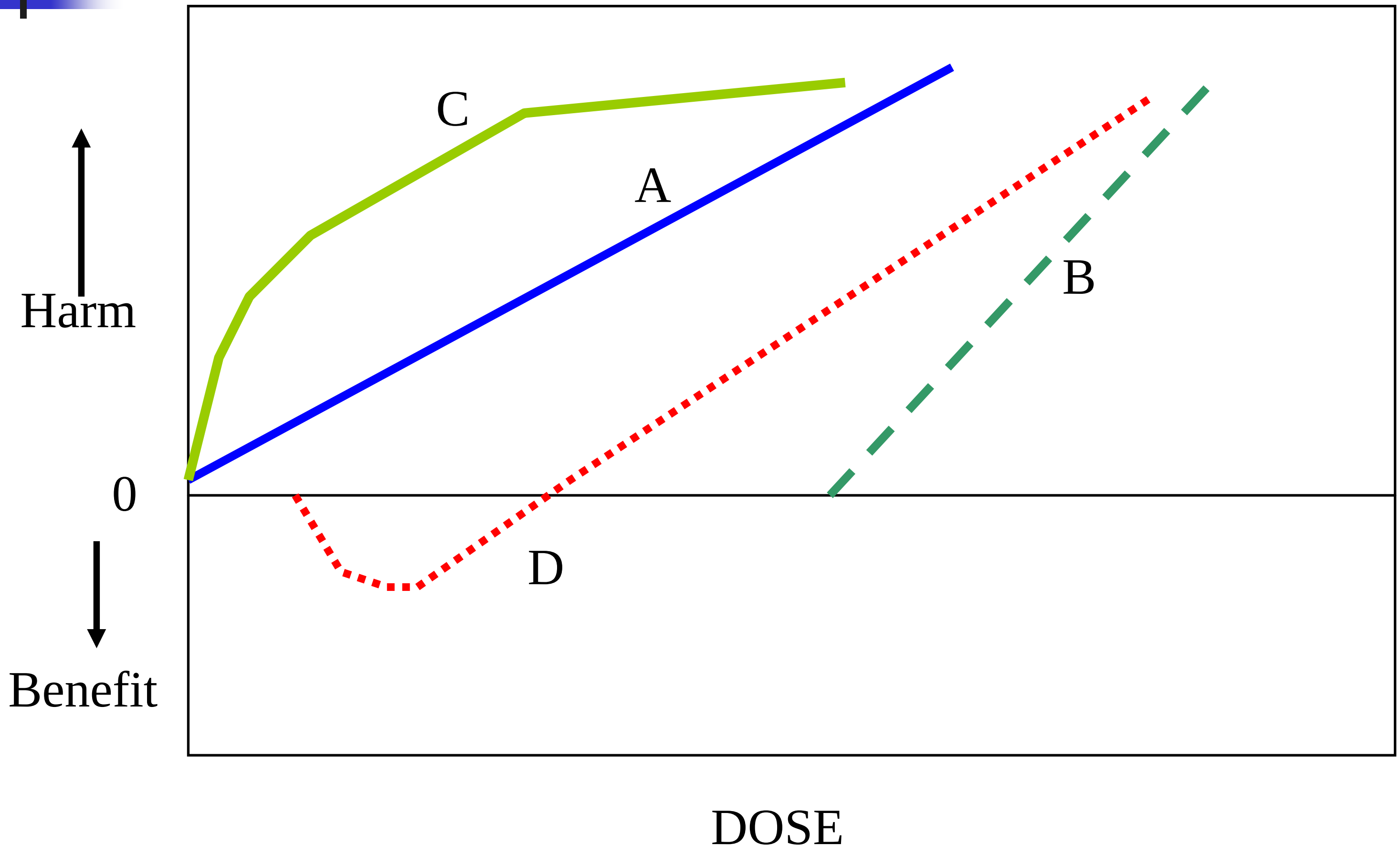
Toxicology

- "*All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy*"

  \- Paracelsus (1493-1541)

- Toxicology: *the science of the nature and effects of poisons, their detection, and treatment of their effects*.

劑量-反應曲線



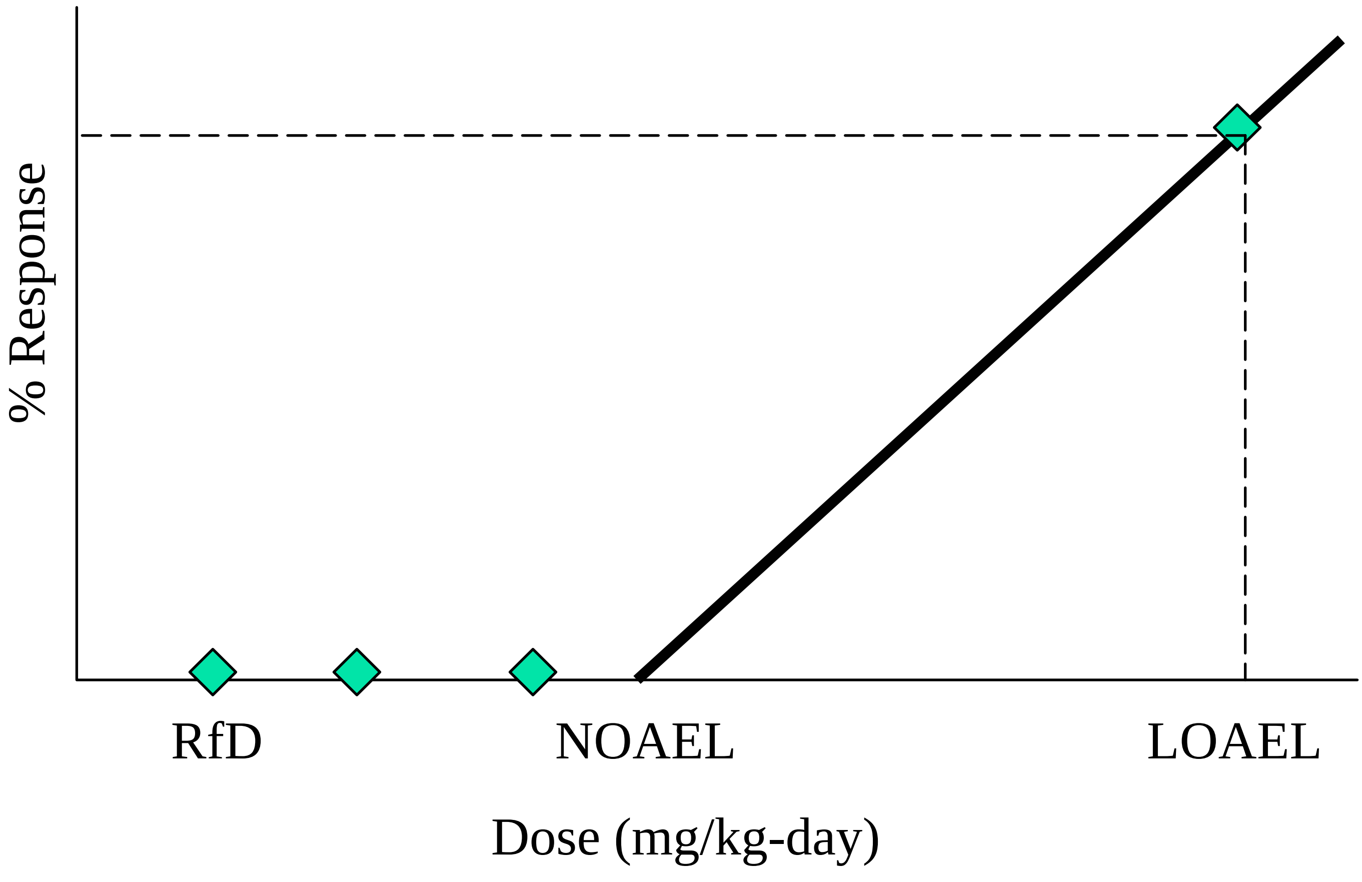
定量毒理學

- 非致癌性
  - Acute toxicity (LD_{50} Lethal dose, mg/g)
  - Chronic toxicity
- 致癌性

Quantifying toxicity - noncarcinogens

- Non-cancer effects
  - Impact the development, size, or functioning of the whole body or body specific organs, but does not lead to the development of malignant cells.
  - “Toxicity threshold” represents the dose below which adverse health effects are not expected to occur.
  - Potential for adverse effects increases as dose increases above toxicity threshold.

Dose-Response Curves (non-carcinogens)



Dose levels (animal studies)

Increasing dose ↓

- NOEL — no-observed effect level
- NOAEL — no-observed-adverse effect level
- LOAEL — lowest-observed-adverse effect level
- MTD — maximum tolerated dose
- LD_{50} — dose which kills 50% of population
- LC_{50} — concentration which kills 50% of population; must include time frame

- Reference dose
  - is an estimate of the daily dose of a chemical that will avoid toxic effects other than cancer
  - The animal dose (NOAEL, LOAEL) is adjusted by uncertainty factors (UF) to allow for differences in sensitivity to chemicals.
    - Human data: UF = 10
    - Animal data:

      UF = 100 (NOAEL), 1000 (LOAEL), 1000 (NOAEL, less data)

- Reference dose (cont.)
  - RfD = NOAEL/UF

    100 mg/kg-day / 100 = 1 mg/kg-day
  - Use RfD to establish allowed concentrations

    allowed C = RfD x body wt / daily intake

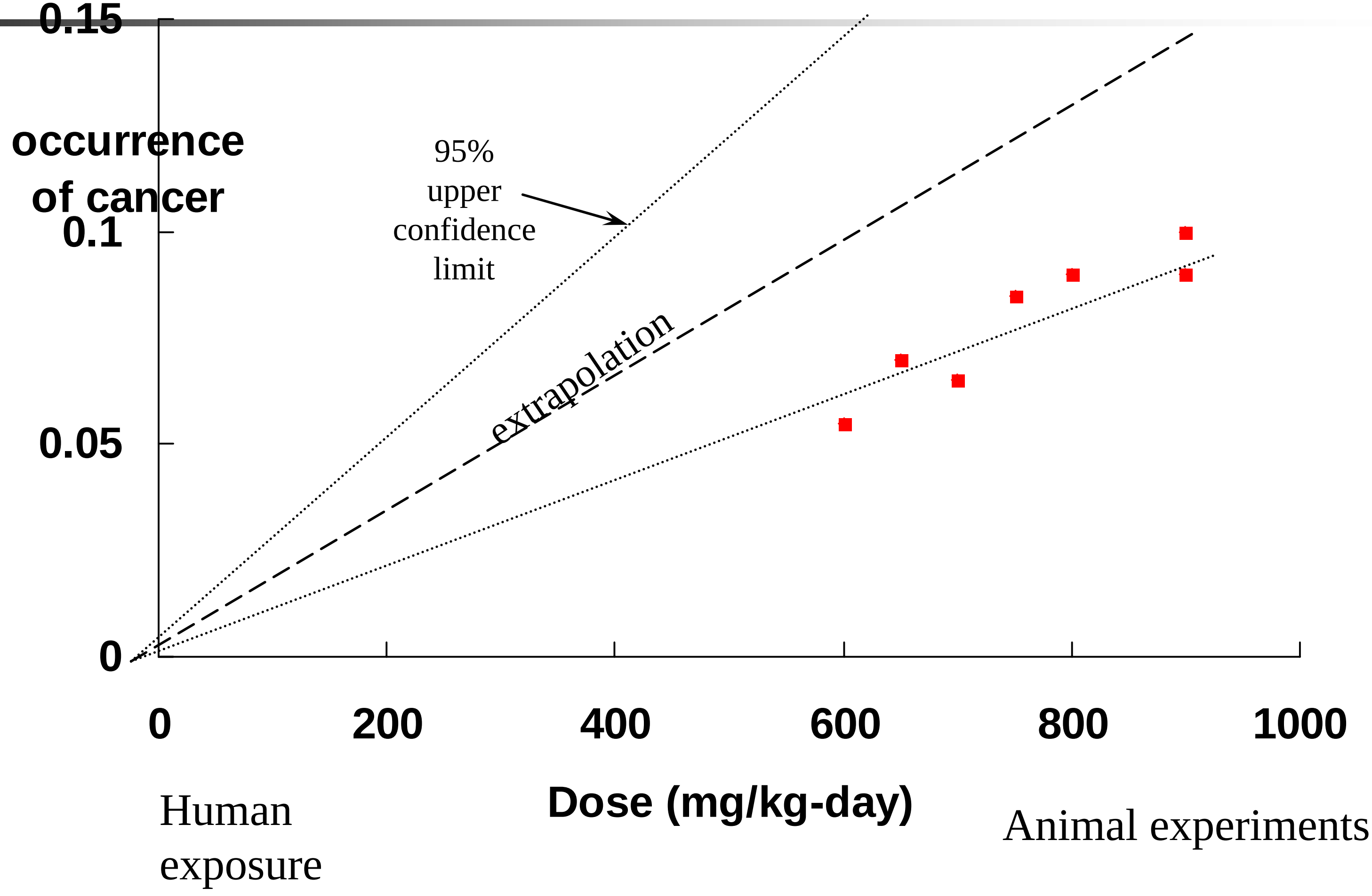
    = 1 mg/kg-day x 70 kg / 2 liters/day

    = 35 mg/l

Quantifying toxicity: carcinogens

- Cancer effects
  - lead to the development of malignant cells
  - “no threshold”: if dose > 0, then response > 0
- Cancer slope factor (SF) (sometimes potency value, PV)
  - incremental risk per unit dose (at low doses)
  - the upper 95th percent confidence limit on the probability of a response per unit intake of chemical of concern over a lifetime

Dose-Response Curves - Carcinogens



EPA carcinogen classification

A - human carcinogen (benzene, Arsenic, Chromium VI, Nickel, Vinyl Chloride)

B1 – Probable human carcinogen (benzo(a)pyrene)

B2 - - less evidence

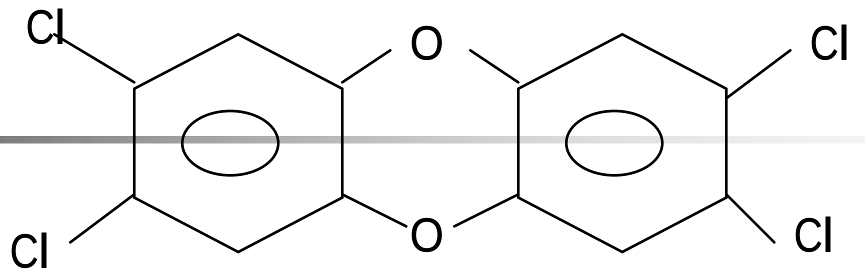
C - Possible human carcinogen (PCE)

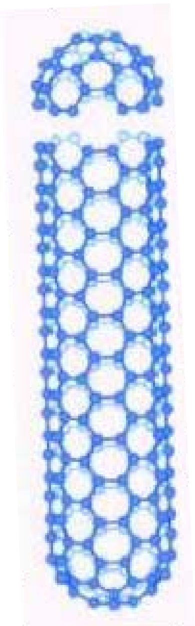
D - not classified as carcinogen (T,E,X, many more)

E - evidence of a non-carcinogen

- Based on “weight of evidence” for cancer:
  positive results in different species, both sexes affected, increased tumors with increased dose, number of tumor sites, decreased time-to-tumor with increased dose, human data (epidemiology)

致癌物



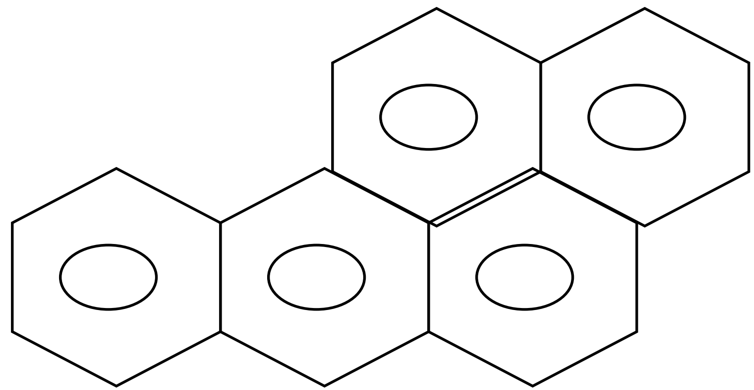


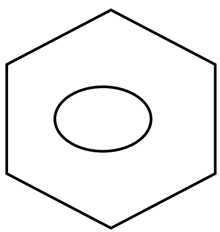
奈米碳管

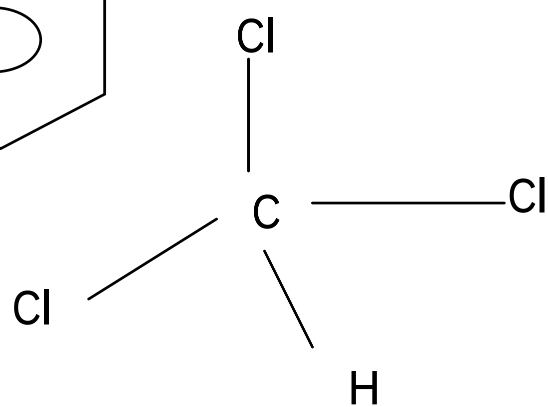
砷

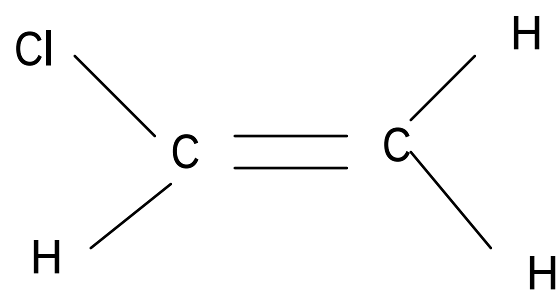
鎳

石綿









Exposure Assessment

Characterize Exposure Setting

- Physical Environment
- Potentially Exposed Populations

Identify Exposure Pathways

- Chemical Source/Release
- Exposure Point
- Exposure Route

Quantify Exposure

Exposure Concentration

Intake Variables

Exposure

Site Assessment

- Identify actual or potential exposure pathways, exposure point concentration,

- Determine concentrations of Contaminants (COC) for all affected media
- Delineate extent of affected media
- Identify site conditions which control COC movement through media

Identify exposure pathways

- Mechanism of transport from source through environment to exposed individual (**receptor**)
- A **complete pathway** has
  - Contaminant source area
  - Environmental medium (e.g., soil, air, water)
  - methods of exposure
    (e.g., ingestion, inhalation, dermal contact)

Exposure Point Concentration

- Modeling and/or actual data for each complete exposure pathway
- **Reasonable maximum exposure** (RME)
  - Maximum (worst case)
  - Reasonable
- Modeling involves subjectivity

Estimation of Chemical Intakes

- Chronic Daily Intake (**CDI**)
  - Daily Intake:
    DI (mg/kg-day) = C (mg/vol) * Intake (vol/day) / body mass (kg)
  - **CDI** = DI averaged over exposure
  - Lifetime average daily dose
    LADD = DI averaged over 70 year lifetime
- Models for various exposure routes
  - Lots of factors, exposures
  - Typical or default values in databases

Estimation of chemical intakes: example

- Air intake - on-site, commercial, adult
  - lifetime = 70 yrs
  - body wt. = 70 kg
  - inhalation rate = 20 m^3/day (2.5 m^3/hr x 8 hr/day)
  - concentration = 0.2 mg/m^3
  - exposure duration = 25 yrs
  - frequency = 250 days/yr
- **DI** =
- **CDI** =
- **LADD** =
  - note: absorbed vs. administered dose

Numerical Estimates of Risk

- Cancer Risk =
  LADD x Slope factor
  - Sum pathways and chemicals (maybe)
  - Greater than 1×10^{-6} is unacceptable (usually)
- Noncancer Hazard Quotient = Total Intake / Ref Dose
  - Greater than 1 is unacceptable

Non-carcinogenic effects

- Compare dose with reference dose (RfD)
  - Hazard Quotient (HQ)

    HQ = Intake/RfD
  - HQ > 1 is unacceptable
  - "Intake" is CDI
    - note: cancer risk uses LADD, non-cancer effect uses CDI
      - note: absorbed vs. administered dose

Noncancerous effects - example

- Assume concentration of Toluene was the same as benzene in previous example:
  - $C_{toluene}$ = 0.2 mg/m^3
  - CDI = 0.039 mg/kg-day
- $RfD_{toluene}$ (inhalation) = 0.11 mg/kg-day
- HQ = (acceptable?)
    - note that the same dose of benzene was unacceptable because of cancer risk
- Acceptable concentration of toluene is concentration which gives reference dose
  - $C_{acceptable} = C_{calculated} / HQ =$

Uncertainties

- Land use, ground water flow, characterization
- Parameter uncertainty and sensitivity
- Quantitative techniques for uncertainty and sensitivity
  - Confidence intervals
  - Monte-Carlo techniques
- Health affects, toxicity parameters