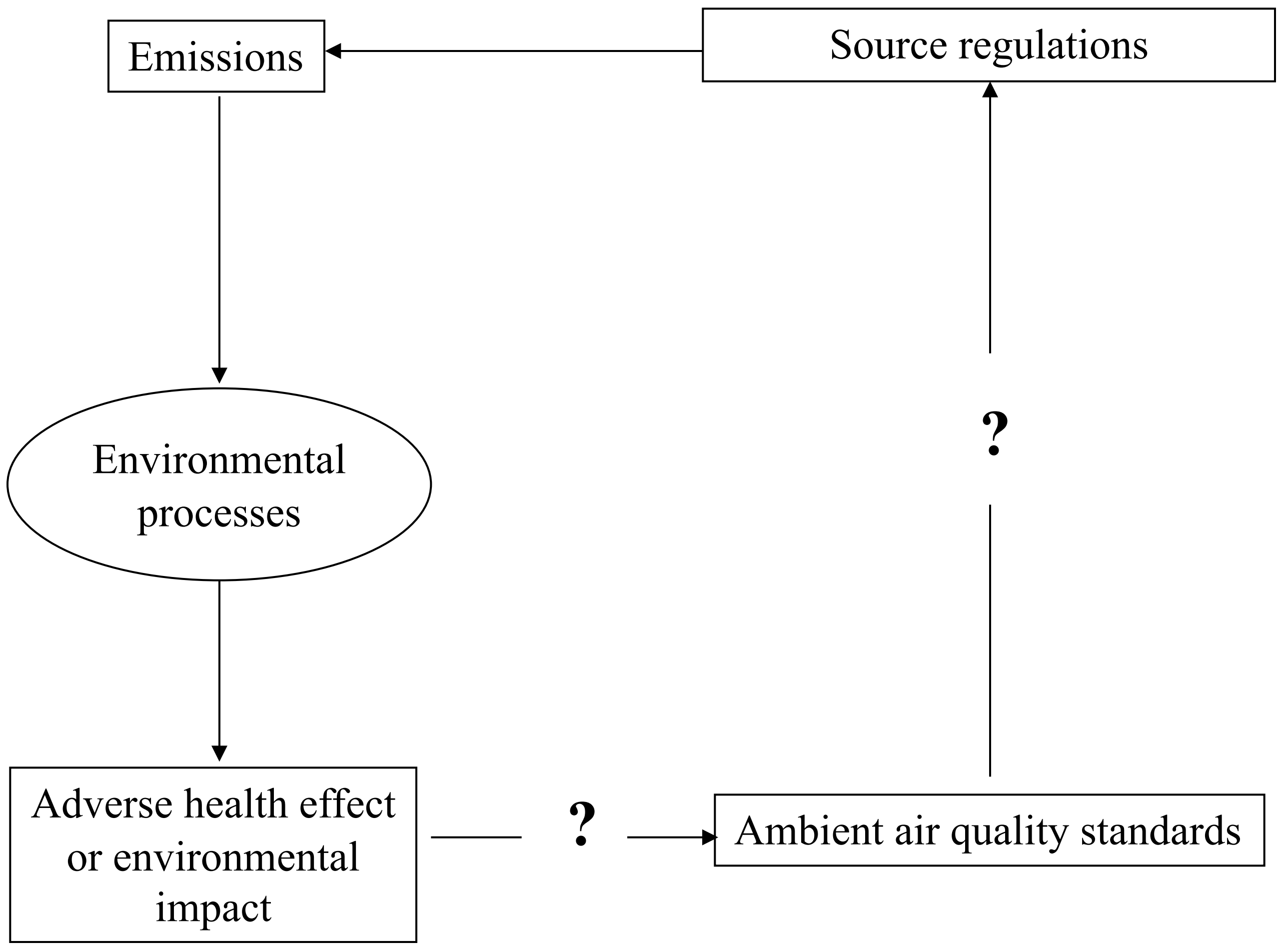
Health Effects of Air Pollution

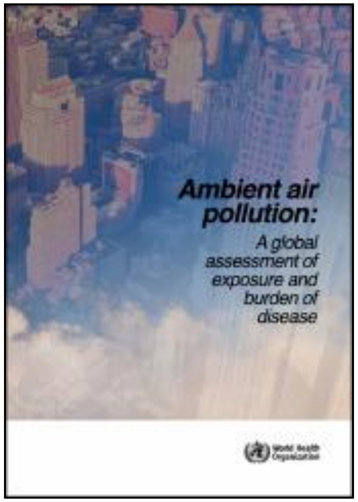
- Identification and characterization of health effects
  - General considerations
  - Toxicology
  - Epidemiology
  - Analysis of health effects
- Health risk assessments

Regulatory Framework



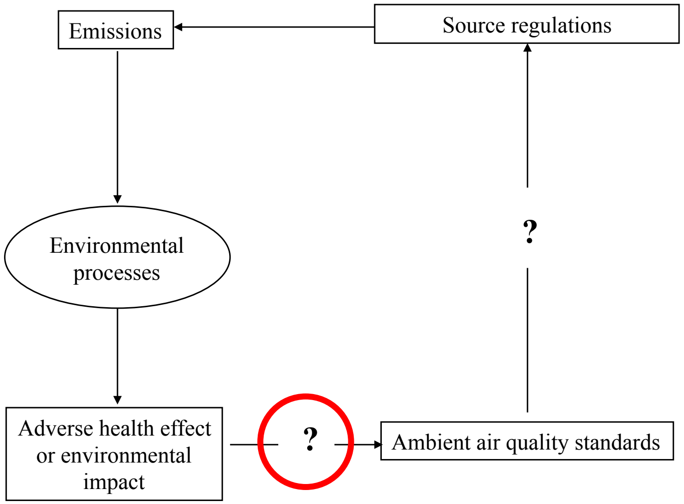
Health Effects of Air Pollution

- Outdoor ambient air pollution kills about **3 million people annually worldwide** (Source : "Ambient air pollution", World Health Organization, 2016).



Health Effects

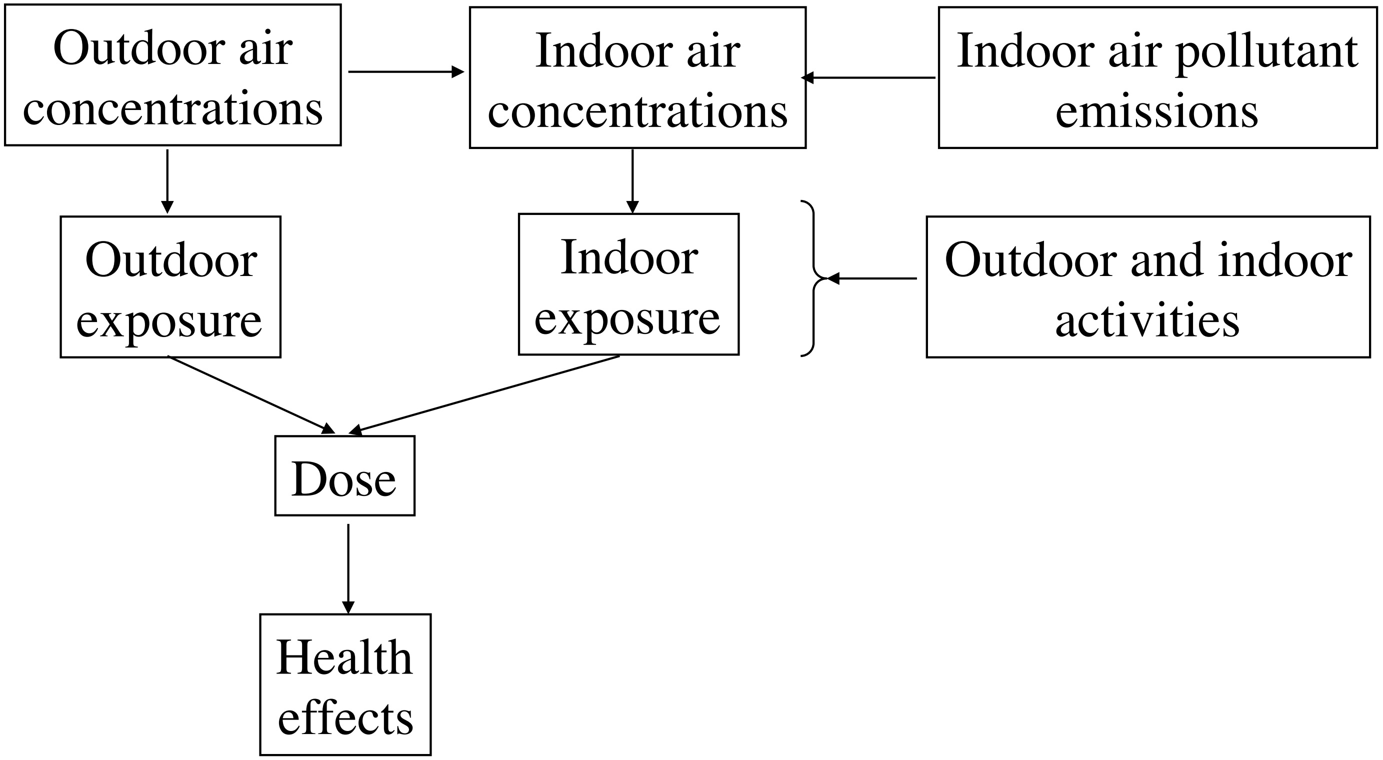
- Exposure and dosimetry
- Toxicology
- Epidemiology
- Analysis of health effects =>
  Ambient air quality standards
  - The relationship between the adverse health effect and the outdoor ambient air pollutant concentration may be difficult to establish and/or to quantify



Exposure

- Exposure to air pollutants includes both outdoor and indoor air pollution.
- Indoor air pollution depends on the penetration of outdoor air pollution indoor and on indoor air pollution sources.
- Most health studies of air pollution focus on outdoor air pollution (for example, to support the development of ambient air quality standards), although a few studies take into account the whole (outdoor + indoor) exposure of individuals.

Exposure


Outdoor air concentrations
Indoor air concentrations
Indoor air pollutant emissions
Outdoor exposure
Indoor exposure
Outdoor and indoor activities
Dose
Health effects

Outdoor and Indoor Exposures

Example: Exposure study of Clayton et al. (Particle Total Exposure Assessment Methodology (PTEAM) study: distributions of aerosol and elemental concentrations in personal, indoor, and outdoor air samples in a southern California community, *J. Exposure Analysis Environ. Epidemiology*, **3**, 227-250, 1993):

- A good correlation ($r = 0.86$) was found between outdoor air concentrations and outdoor exposure
- No significant correlation ($r = 0.05$) was found between outdoor air concentrations and indoor exposure
- A weak correlation ($r = 0.37$) was found between outdoor air concentrations and total (outdoor + indoor) exposure

Dosimetry of Particulate Air Pollutants
Influence of Particle Size

- Coarse particles greater than about 10 µm in diameter are typically not inhaled.
- PM_{10} particles enter the respiratory system (i.e., respirable particles).
- Coarse particles (those with a diameter between about 2.5 and 10 µm) are captured mostly within the upper airways (nose, mouth, upper respiratory tract).
- Fine particles (those with a diameter between about 0.1 and 2.5 µm) and ultrafine particles (those with a diameter less than 0.1 µm) reach the lungs.
- Ultrafine particles deposit very efficiently within the lungs.
- Fine particles deposit partially within the lungs, but the majority of those particles exit during exhalation.

Toxicology

- Toxicology leads to some understanding of the processes that are the cause of adverse health effects.
  - In vitro studies
    - They are conducted with cell cultures
  - In vivo studies
    - Clinical studies conducted with human beings
    - Laboratory studies conducted with animals (some extrapolation to human beings is needed)

Toxicology
In Vitro Studies

- Studies conducted with cell cultures
- They allow one to study the fundamental biological processes.
- Example: the Ames test (developed by Professor Bruce Ames, University of California at Berkeley), which is used to identify mutagenic chemical substances.
- In air pollution, in vitro studies may lead to the identification of inflammatory processes, oxidation processes, and the transfer of particles into cellular tissues.

Toxicology
Clinical Studies with Individual Human Beings

- The exposure to selected pollutants is controlled in the laboratory.
- The air inhaled may contain a specific air pollutant or may be a sample of polluted air.
- Typical tests include measuring the pulmonary function and/or various parameters related to cardiac performance.

Toxicology
Pros and Cons

- Advantages
  - For clinical studies conducted with human beings, the results are directly useable for public health applications.
  - Specific air pollutants may be used.

- Shortcomings
  - The number of individuals included in a study is small.
  - The most sensitive individuals cannot be included in such studies.
  - Exposure duration is short.
  - Air pollutant concentrations may be greater than those observed in the atmosphere.
  - Specific air pollutants are used without their possible interactions with other pollutants (except in studies where actual polluted air is used).
  - Specialized laboratories are needed.

Toxicology
Animal Studies

- Advantages: They provide data that might not be available from studies conducted with human beings.
  - Greater concentrations
  - Longer exposure durations
  - Use of sensitive animals
  - Autopsies following death

- Shortcomings:
  - The results must be extrapolated from the animal to Man (e.g., using respiratory system models).
  - Ethical issues

Epidemiology

- Analysis of the effect of air pollution on public health
- Statistical relationship between the air pollution level and the health effect
- Identification of adverse health effects among sensitive individuals

Epidemiology
Different Types of Studies

- Population (ecological studies)
  - The statistical association between the health effects and the air pollution is analyzed for an entire population (e.g., for a city).
- Cohort
  - The exposure of a group of individuals (the cohort) is estimated either directly or indirectly, and is compared to the health effects.
- Case-control groups
  - A comparison is conducted between a group that shows some adverse health effect (the case group) and a control group that does not show this specific health effect.
  - Since the individuals showing some health effect are identified from the start, a case-control study can use a smaller number of individuals than a cohort study (thus the associated costs are less).

Epidemiology
Different Types of Studies

- Cross-sectional studies
  - Comparison of adverse health effects between different regions (e.g., near and far away from a highway)

- Longitudinal studies
  - Analysis of adverse health effects as a function of time (e.g., before, during, and after an air pollution episode)
  - Only for acute exposure

Epidemiology
Different Types of Studies

- Mortality
  - Number of deaths
  - Cause of death (respiratory, cardio-vascular, cancer…)

- Morbidity
  - Emergency admissions for example
  - Symptoms (asthma attacks, cardio-vascular problems…)

Epidemiology
Factors to Take into Account

- Age
- Climate and meteorology (temperature)
- Social-cultural aspects
- Profession
- Education
- Activities
- Individual behavior (e.g., smoking)
- Etc.

Epidemiology
Statistical Association

- The epidemiological study provides a statistical association between exposure (or its proxy, i.e., outdoor concentration) and the health effect. It is not a cause/response relationship.
- This association may be more or less likely.
- Importance of this statistical relationship
  - Strength of the statistical relationship (correlation)
  - Constance among several studies (the results of several studies are similar).
  - Specificity (a cause is associated with a single effect).
  - Temporality (the exposure occurs before the effect).
  - Plausibility (the statistical relationship is consistent with the relevant biological data).

Epidemiology
Risk Metrics

- Examples of some metrics used in epidemiology:
  - Relative risk, RR, used for example in cohort studies and ecological studies
  - The odds ratio, OR, used in case-control studies
  - Usually: $RR \approx OR$

Epidemiology
Uncertainties

- In an epidemiological study, there is a large number of uncertainties, which must be taken into account when calculating *RR* (or *OR*).

- Therefore, error bounds must be associated with the estimated risks (for example, the 95 % confidence intervals).

Epidemiology Limitations

- The biological mechanism is not identified.
- The relationship between exposure and the outdoor air pollutant concentrations is uncertain.
- The effects of other air pollutants may affect the results of the analysis.

Epidemiology
Pros and Cons

- Advantages
  - An epidemiological study pertains to the effects of air pollution on actual public health situations.
  - Sensitive individuals are included.

- Shortcomings
  - Problem of interactions among various air pollutants
  - Confounding effects due to other factors: meteorology, socio-cultural factors, etc.
  - It is a statistical association, not a cause-to-effect relationship.

Examples of Adverse Health Effects of some Air Pollutants

Pollutant	Health effects
Lead	Mental retardation on children and other effects
Carbon monoxide	Intoxication (carboxyhemoglobin => hypoxia)
Sulfur dioxide	Respiratory effects
Nitrogen dioxide	Respiratory effects
Ozone	Respiratory effects
Fine particles	Cardiovascular and respiratory effects
Benzene	Cancer (leukemia)

Health Effects => Regulations

Toxicological and/or epidemiological => regulations characterized by values not to be exceeded (or exceeded a limited number of times)

For example:

- Concentration values below which it is assumed that there are no adverse health effects, if possible with a margin of safety: CO, NO_2, SO_2, O_3

- For pollutants without a concentration threshold (for example, carcinogenic chemicals): a criteria considered to be sufficiently protective of public health is used; for example, excess cancer risk due to benzene of 10^{-5}.

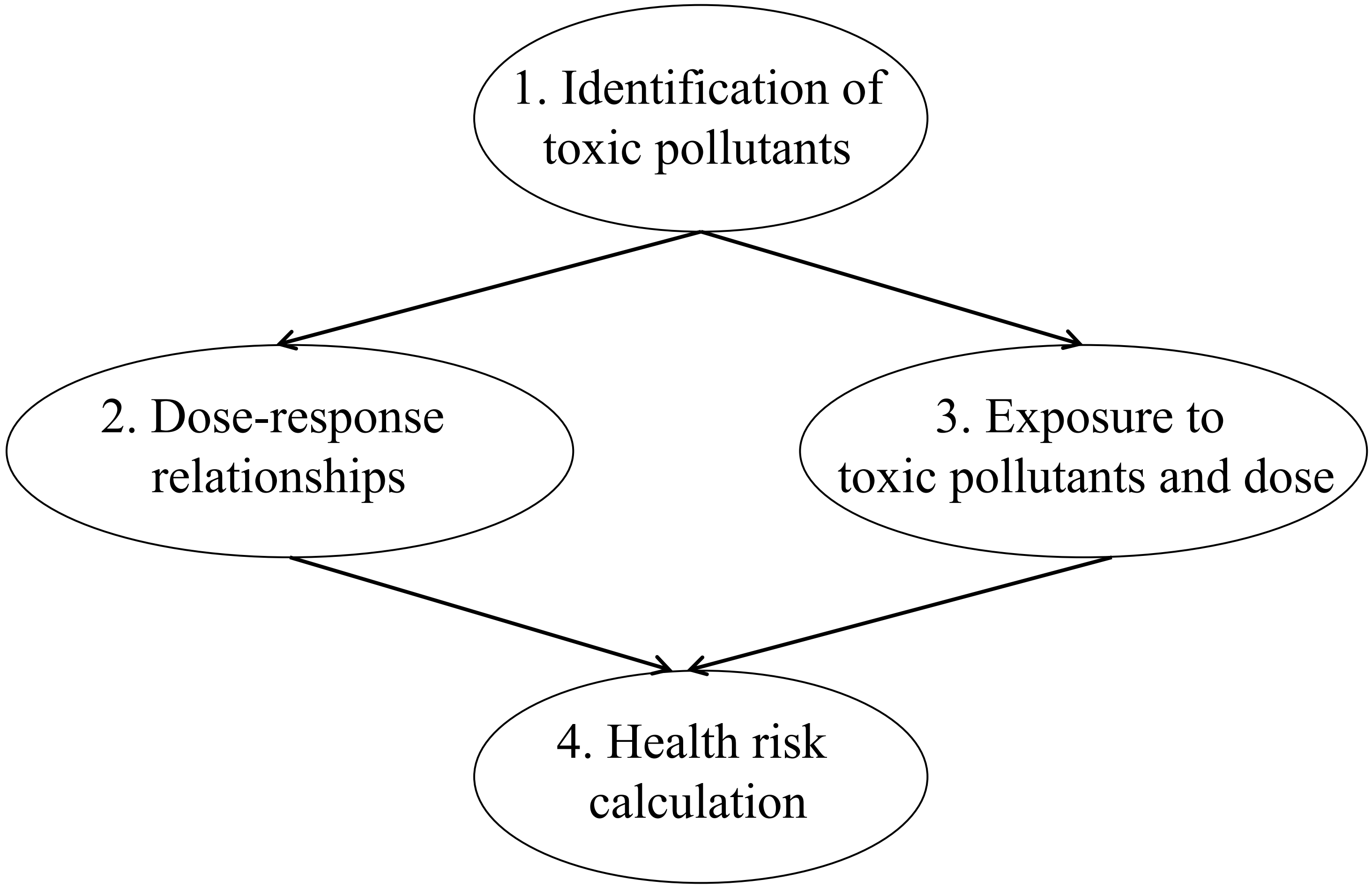
Health Risk Assessment

- Health risk assessments (HRA) typically use simple dose-response relationships.

- An HRA addresses two distinct types of health effects:
  - Cancer
  - Other health effects

- and two exposure durations:
  - Chronic exposure (long term)
  - Acute exposure (short term)

Health Risk Assessment Approach with Four Steps



Health Risk Assessment
1. Risk Identification

- Which chemicals present a health risk?
  - List of chemicals emitted by the air pollution source(s)
  - List of chemicals with adverse health effects

↓

  - List of pollutants that must be included in the HRA

Health Risk Assessment
2. Dose-Response Relationships

- For non-carcinogenic pollutants, it is assumed that there is a concentration or dose below which there is no adverse health effect. This value is defined as a **reference concentration** (*RfC*) for the inhalation exposure pathway and as a **reference dose** (*RfD*) for the ingestion and dermal absorption exposure pathways.

- *RfC* and *RfD* values are available in databases such as IRIS (U.S. EPA) and OEHHA (California).

- The use of recommended values from the World Health Organization (WHO) and of air quality regulations must be done with caution and may not be recommended.

Health Risk Assessment
2. Dose-Response Relationships

- For carcinogenic pollutants, it is assumed that there is no threshold and that the dose-response relationship is linear. The slopes of these relationships are the **unit risk factor** (*UR*) for concentrations and the **cancer slope factor** (*CSF*) for doses. They correspond to the increase in cancer risk to a an increase in a unit concentration or unit dose, respectively.
  - *UR* $(\mu g/m^3)^{-1}$ for a concentration (inhalation)
  - *CSF* $(mg/kg/an)^{-1}$ for a dose (ingestion or dermal absorption)

- *UR* and *CSF* values are available in databases such as IRIS (U.S. EPA), IARC (WHO), and OEHHA (California).

Health Risk Assessment
3. Calculation of Exposure and Dose

- For each pollutant and each exposure duration, the absorbed dose is calculated:
  - Dose = mass of pollutant absorbed per kg of individual per unit time (for example, g per kg per year)
  - Dose: inhalation, ingestion, and dermal absorption
  - Microenvironments and/or individual activities can be taken into account.
  - Two types of calculations:
    - Individual or population at a given location (using average or maximum exposure)
    - Individual or population moving through different microenvironments
- For inhalation, it is assumed that one breaths 20 m^3 of air per day and one may then calculate the concentration (instead of the dose).

Health Risk Assessment
4. Calculation of Health Risk

- For non-carcinogenic health effects, the **hazard quotient** is used to quantify the risk:
- For the inhalation pathway (j = 1), the quotient is calculated using concentrations

  HQ_{i1} = calculated concentration of pollutant i / RfC_i
- For the ingestion and dermal absorption pathways (j = 2 or 3), the quotient is calculated using the doses:

  HQ_{ij} = calculated dose / RfD_{ij}
- Next, for each exposure pathway j, the **hazard index**, *HI*, which is the sum of the hazard quotients, HQ_{ij}, of the individual pollutants i, is calculated:

  $HI_j == \Sigma\, HQ_{ij}$
- Finally, an overall hazard index may be calculated by adding the hazard indexes of the three exposure pathways (inhalation, ingestion, and dermal absorption).
- If $HI < 1$, there is no health risk. If $HI > 1$, there may be some health risk.

Health Risk Assessment
4. Calculation of Health Risk

- For carcinogenic effects, the dose-response function is assumed to be linear and the **individual excess risk**, R_{Hi}, which corresponds to a probability of getting cancer, is calculated as follows for inhalation (using concentrations) and the other exposure pathways (using doses for ingestion and dermal absorption) is calculated for each pollutant *i* and exposure pathway *j* as follows:

  R_{Hi1} = concentration (µg/m^3) x UR_i (µg/m^3)$^{-1}$

  R_{Hij} = dose (mg/kg/an) x CSF_{ij} (mg/kg/an)$^{-1}$; $j = 2$ or 3

- Next, the individual excess risk is calculated by summing over all pollutants *i* and over all exposure pathways $j = 1$ to 3:

  $R_H = \Sigma \Sigma R_{Hij}$

Health Risk Assessment
4. Calculation of Health Risk

- Typically, the cancer risk is considered acceptable if it is less than a value ranging from 10^{-6} (one per million) to 10^{-5} (one per hundred thousand) for chemical pollution and 10^{-4} (one per ten thousand) for radioactivity.

- For a health risk assessment conducted over a large area (e.g., city), the cancer burden is calculated: it is the number of people who will get cancer due to air pollution, i.e., the cancer risk multiplied by the population. Typically, it should be less than 1, i.e., less than one person should get cancer because of air pollution.

- One considers that there is no non-carcinogenic risk if $HI < 1$. If $HI > 1$, the calculation can be refined by calculating *HI* for each target organ. If the organ-specific *HI*'s are all less than 1, then one may consider that there is no risk.

Health Risk Assessment
4. Estimation of Uncertainties

- In a health risk assessment, one must also estimate the uncertainties associated with the HRA calculations and input data. This uncertainty analysis may be done qualitatively (i.e., some discussion of the major sources of uncertainties is provided) or quantitatively. In the latter case, a probabilistic analysis is performed that takes into account the probability distribution functions of the input data, those of the parameters of the various models used in the calculations, and the uncertainties associated with the model formulations.

Example: Number of Cancer Cases in the Paris Region due to Air Pollution

- Carcinogenic pollutants measured in the ambient air:
  - Volatile organic compounds: benzene, toluene, xylenes, ethylbenzene, 1,3-butadiene, formaldehyde, acetaldehyde
  - Semi-volatile organic compounds: benzo(a)pyrene
  - Metals: lead, arsenic, cadmium, nickel
  - Diesel particles
- Carcinogenic risk due to air pollution (urban background):
  - 7×10^{-4} with diesel particles (UR_i of OEHHA)
  - 4×10^{-5} without diesel particles (due mostly to aldehydes, 1,3-butadiene, and benzene)
  - Non acceptable ($> 10^{-5}$)
- Total carcinogenic risk (all causes): 0.40

Example: Number of Annual Deaths in the Paris Region due to PM Air Pollution

- Relationship between mortality (relative risk, *RR*) and PM concentration ($\Delta C = \Delta\ [PM_{2.5}]$):

$$\ln(RR_{\Delta C}) = \beta_S\ \Delta C$$

$RR_{\Delta C} = 1.06$ for $\Delta C = 10\ \mu g/m^3$ (Hoek et al., 2013)

- Let's assume that the annual $PM_{2.5}$ concentration in Paris ($15\ \mu g/m^3$) is reduced to the concentration recommended by the Word Health Organization (i.e., $10\ \mu g/m^3$)

$$\Delta\ [PM_{2.5}] = -\ 5\ \mu g/m^3 \text{ (decrease from 15 to 10 } \mu g/m^3\text{)}$$

Example: Number of Annual Deaths in the Paris Region due to PM Air Pollution

- The fraction of annual deaths due to air pollution (here, $PM_{2.5}$) is calculated using the relative risk (RR).

$$\text{Fraction of annual deaths due to } PM_{2.5} = 1 - \exp\left(\frac{\ln(1.06)(10-15)}{10}\right) \approx 2.9\%$$

- It is the etiologic fraction (i.e., the fraction of the risk due to air pollution).

- 70 000 deaths per year in the Paris regino => ~2 000 deaths per year could be avoided if the $PM_{2.5}$ concentration were to be reduced to 10 μg/m^3.

- Note that there is some uncertainty associated with β_s : RR is in the range of 1.04 to 1.08 for ΔC = 10 μg/m^3 => between 1 360 and 2 640 deaths per year could be avoided.

Mortality due to Air Pollution

- It is due mostly to:
  - Cardiovascular risks ($PM_{2.5}$)
  - Respiratory risks (PM, O_3, NO_2, and SO_2)

- Cancer risks due to air pollution are low compared to all other causes of cancer (for example, < 0.2 % of all causes of cancer in Paris). However, they are sufficiently high to be considered unacceptable by air quality agencies (for example, relative risk > 10^{-5} in Paris).