

Human Exposure Assessment and Risk Assessment (part 1)

Bengt Melsäter, M.Sc.
Toxicologist
bengt.melsater@kemi.se

ITP299EU 2014: Strategies for Chemicals Management
September 2014

CONTENT

- Human Exposure Assessment**
- Human Risk Assessment**
- Risk assessment in REACH (EU)**
- Risk assessment of pesticides in EU**
- Information on databases/available assessments**
- Further Links**

Human Exposure Assessment

Definitions

Exposure

- Concentration or amount of a particular agent that reaches a target organism, system, or (sub)population in a specific frequency for a defined duration

Exposure assessment

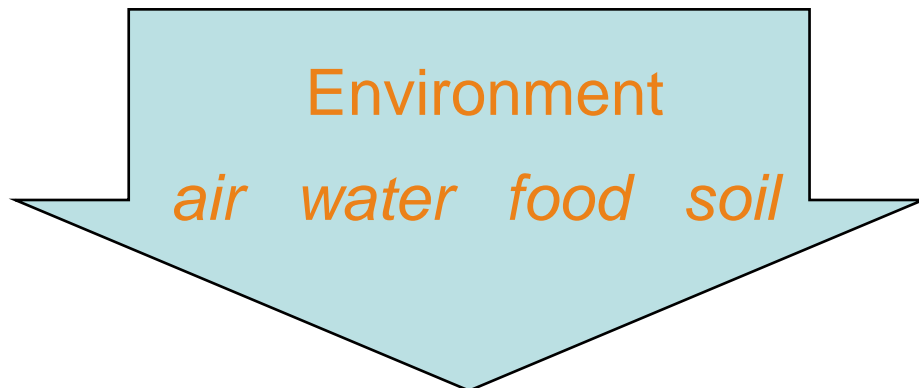
- Evaluation of the exposure of an organism, system, or (sub)population to a chemical substance (and its derivatives)

Exposure scenario

- A set of conditions or assumptions about sources, exposure pathways, amounts or concentrations of agent(s) involved, and exposed organism, system, or (sub)population (i.e., numbers, characteristics, habits) used to aid in the evaluation and quantification of exposure(s) in a given situation

IPCS Risk Assessment Terminology (WHO, 2004)

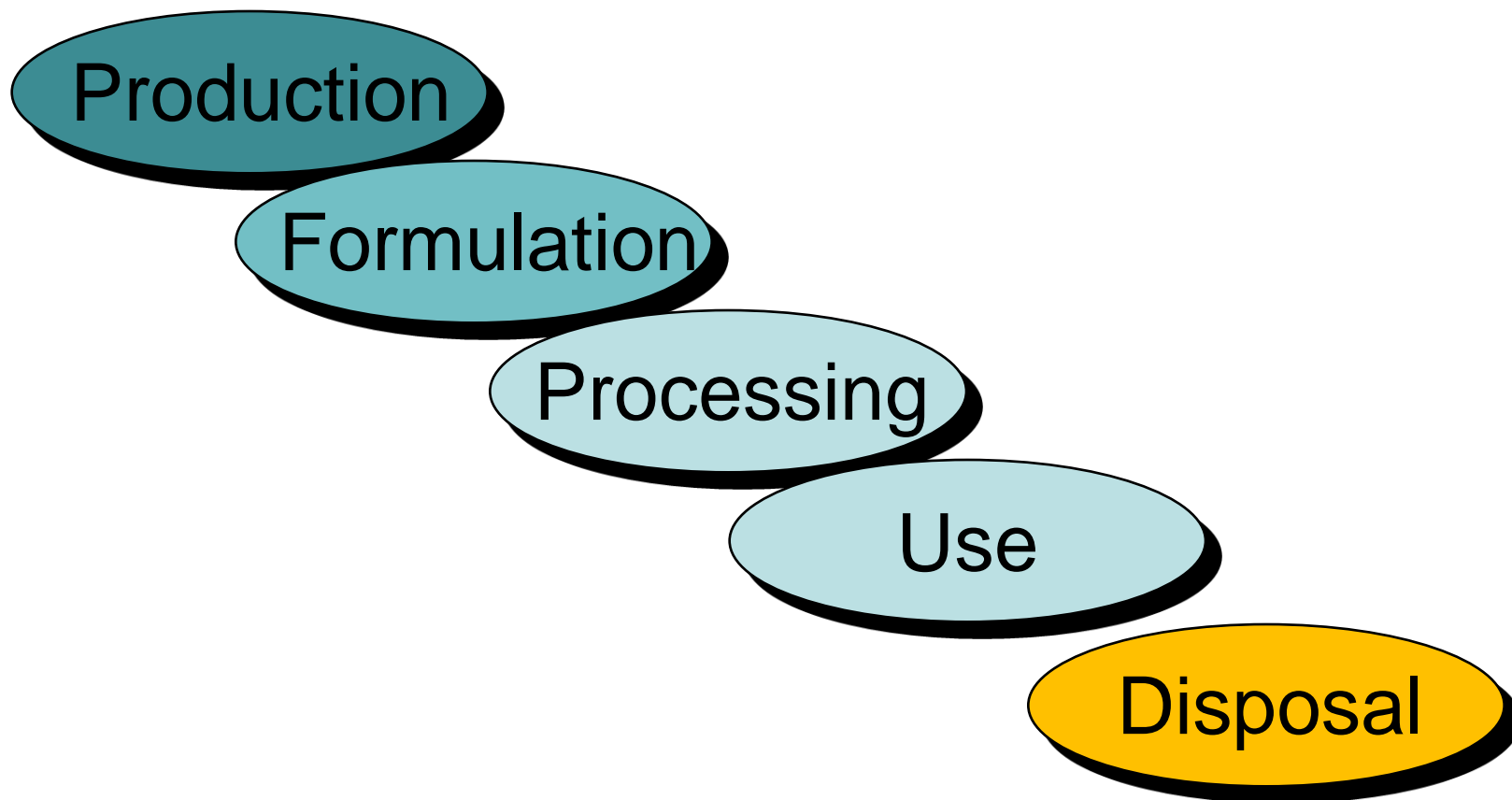
Exposure pathways



oral inhalation dermal



Emissions – life cycle stages

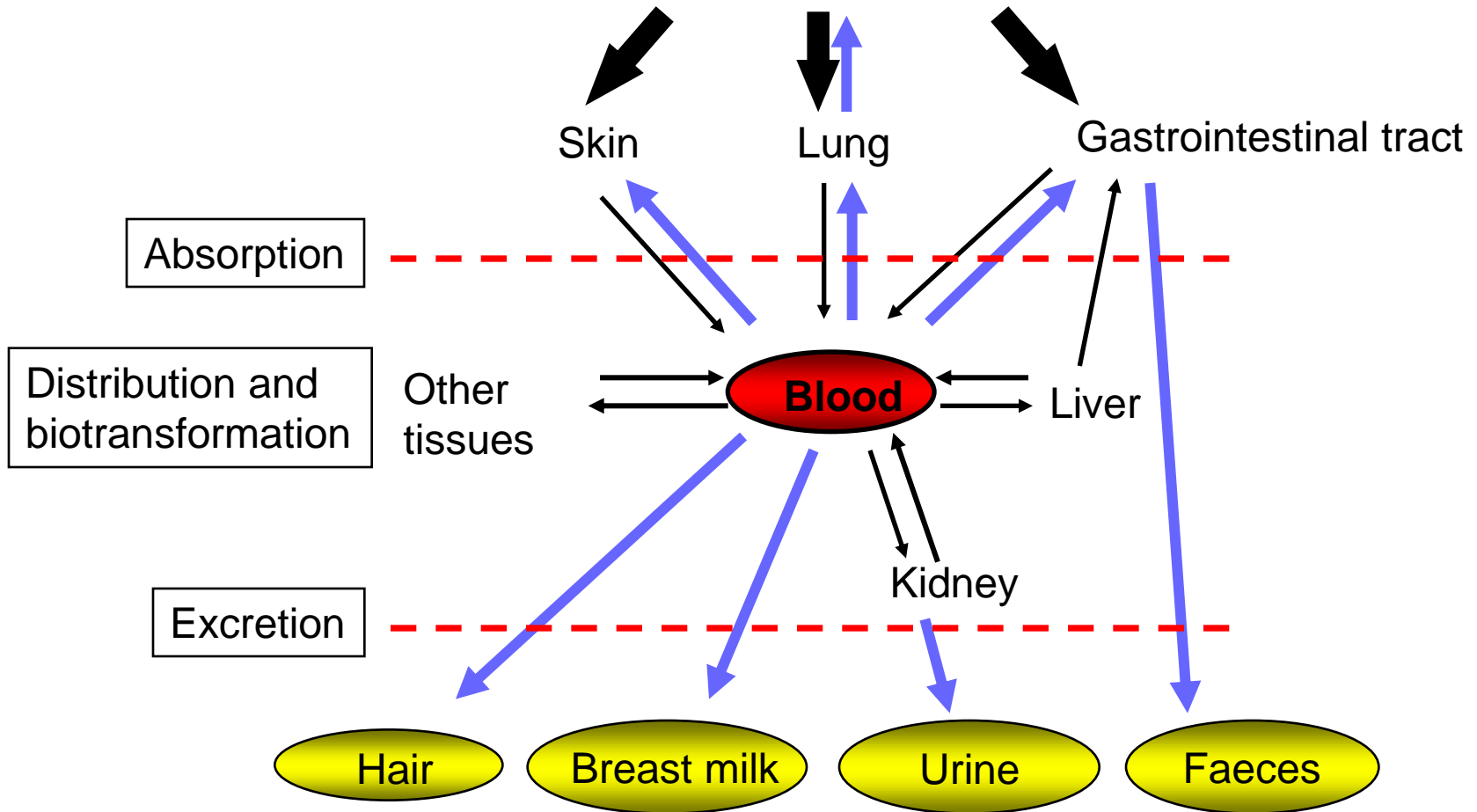


Types of exposure

- **Acute exposure**
 - accidental exposure
 - Acute toxic dose
- **Intermittent exposure**
 - e.g. work place
 - Recovery
- **Chronic exposure**
 - e.g. ambient air, drinking water
 - Cumulative dose



Environmental agents/substances



Dose

The amount of a substance that enters a target in an organism after crossing an **exposure surface** or **absorption barrier**

- **Exposure surface**
 - Skin surface, respiratory tract, gastrointestinal tract
 - *Intake dose*
- **Absorption barrier**
 - Skin, respiratory tract lining, gastrointestinal tract wall
 - *Absorbed dose*

Qualitative assessment



Non-exposed



Exposed

Quantitative assessment

(Concentration x contact volume)/time

- Concentration of a substance in an environmental media
 - Air, drinking water, food, soil, dust, products
- Contact volume
 - volume of air inhaled, (m³)
 - Amount of food (g/kg bw per day)
 - Amount of drink (l/kg bw per day)
 - Amount adhered to the skin (g/cm²)
- Time
 - Intermittent, occasionally, hour, 24 h, fetal stadium, life time

$$E = \int_{t_1}^{t_2} C(t) dt$$

E= exposure

C(t)= exposure concentration

t₁-t₂=duration of exposure

Exposure assessment



Exposure models



Environmental monitoring



Personal exposure monitoring



Biomonitoring

- *Absorbed dose*
- *Body burden*
- *Target tissue concentration*
- *Biologically effective dose*

Exposure data

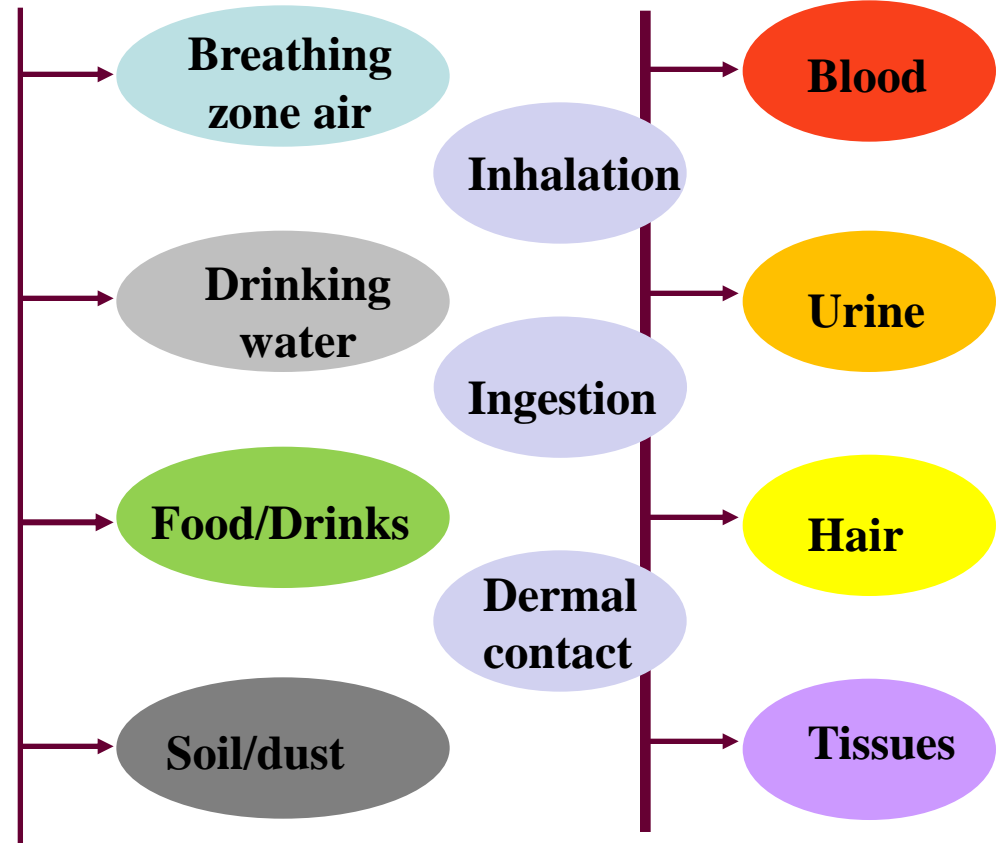
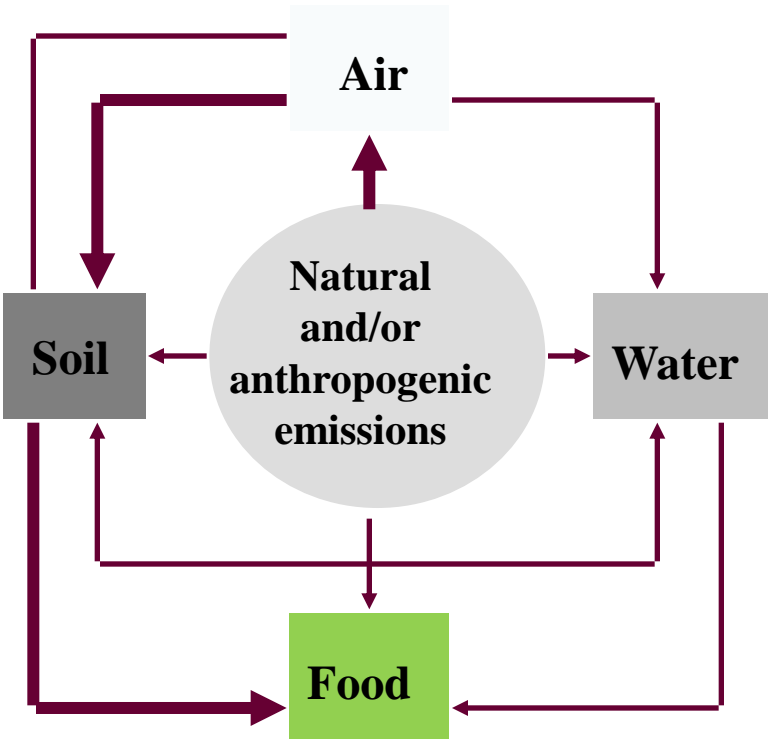
- **Primary data**
 - Measurements, monitoring etc.
- **Secondary data**
 - default values from exposure models
 - Compare modelled and measured data
 - Check relevance and reliability of measured data

Environmental media

Exposure media

Biological media

Absorption barrier



Environmental monitoring

Personal monitoring

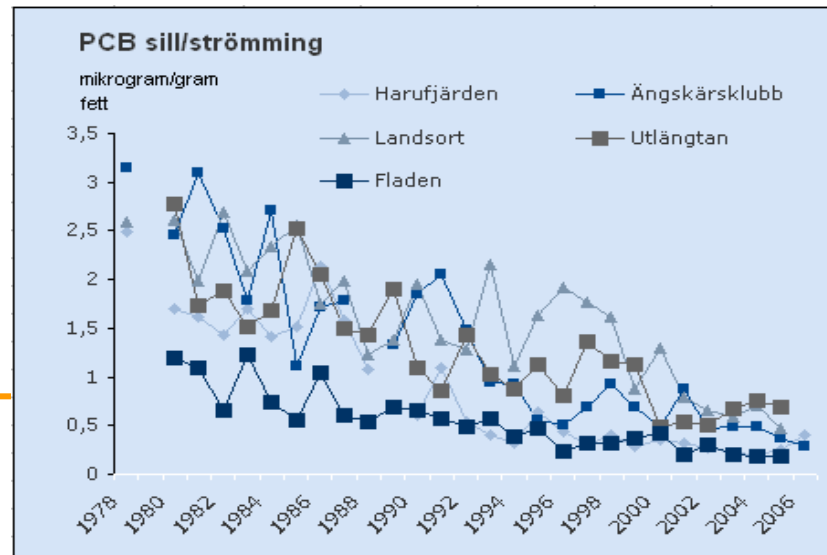
Biomonitoring

Environmental monitoring

- Concentration of specific chemicals in environmental media: - air, water, food, soil, dust
- Assumptions on physical contact with environmental media

➔ Assessment of approximate human exposure

Levels of PCB in Herring



Personal monitoring

- Air
 - Breathing zone air
- Food and drinking water
 - Food frequency questionnaires
 - 24-h recall
 - Duplicate portion technique
- Ingestion of non-food substances
 - Hand-to-mouth activity
- Dermal exposure
 - Hand wipes
 - Contact rates



Questionnaires

- **Individual characteristics**
 - Age, Gender, Living conditions, Work conditions, Socio-economic factors
- **Exposure factors**
 - Time spent indoors/outdoors/commuting to work
 - Daily intake of water (tap/bottled)/food/drinks
- **Life-style and activity factors**
 - Smoking, Drinking, Food, Physical activity

Diaries

- **Time-activity patterns**
 - Where and how did you spend your time, e.g. every 15 minutes of a day or week
- **Annoyance**
 - Generally in relation to air pollutant concentrations or noise

Biomarkers

- Biomarkers of exposure
 - Indicator of exposure and the resulting dose
 - *e.g. blood levels*
- Biomarkers of effects
 - A biochemical change of potential toxicological importance
 - *e.g. proteinuria*
- Biomarkers of sensitivity
 - Indicator of individual sensitivity
 - *e.g. enzyme polymorphism*

Exposure models



Workers

- EASE (Estimation and Assessment of Substance Exposure)

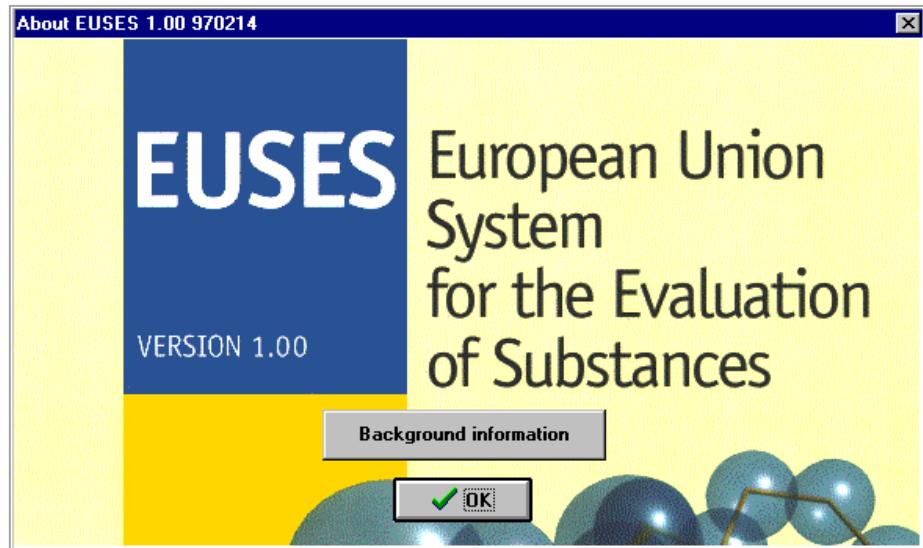
Consumers

- CONSEXPO (CONSUMER EXPOSURE)
 - contact, exposure, uptake
- THERdbASE (Total Human Exposure Related Data Base and Advanced Simulation Environment)
 - simulates different agents
- USEPA household exposure models
- SCIENS - volatile substances
- DERMAL - dermal exposure

Exposure models – indirect exposure

EUSES (European Union System for the Evaluation of Substances)

- Integrated exposure measurement - total uptake of a substance via:
 - food
 - drinking water
 - air
 - soil
- Available for download at



http://ihcp.jrc.ec.europa.eu/our_activities/health-env/risk_assessment_of_Biocides/euses/euses

Factors to consider

Physiological factors

- Age
- Gender
- Body weight
- Skin surface area
- Physical condition
- Disease
- Genetics

Behavioural factors

- Time-activity patterns
- Life-style factors
- Socio-economics
- Nutritional status
- Physical activity

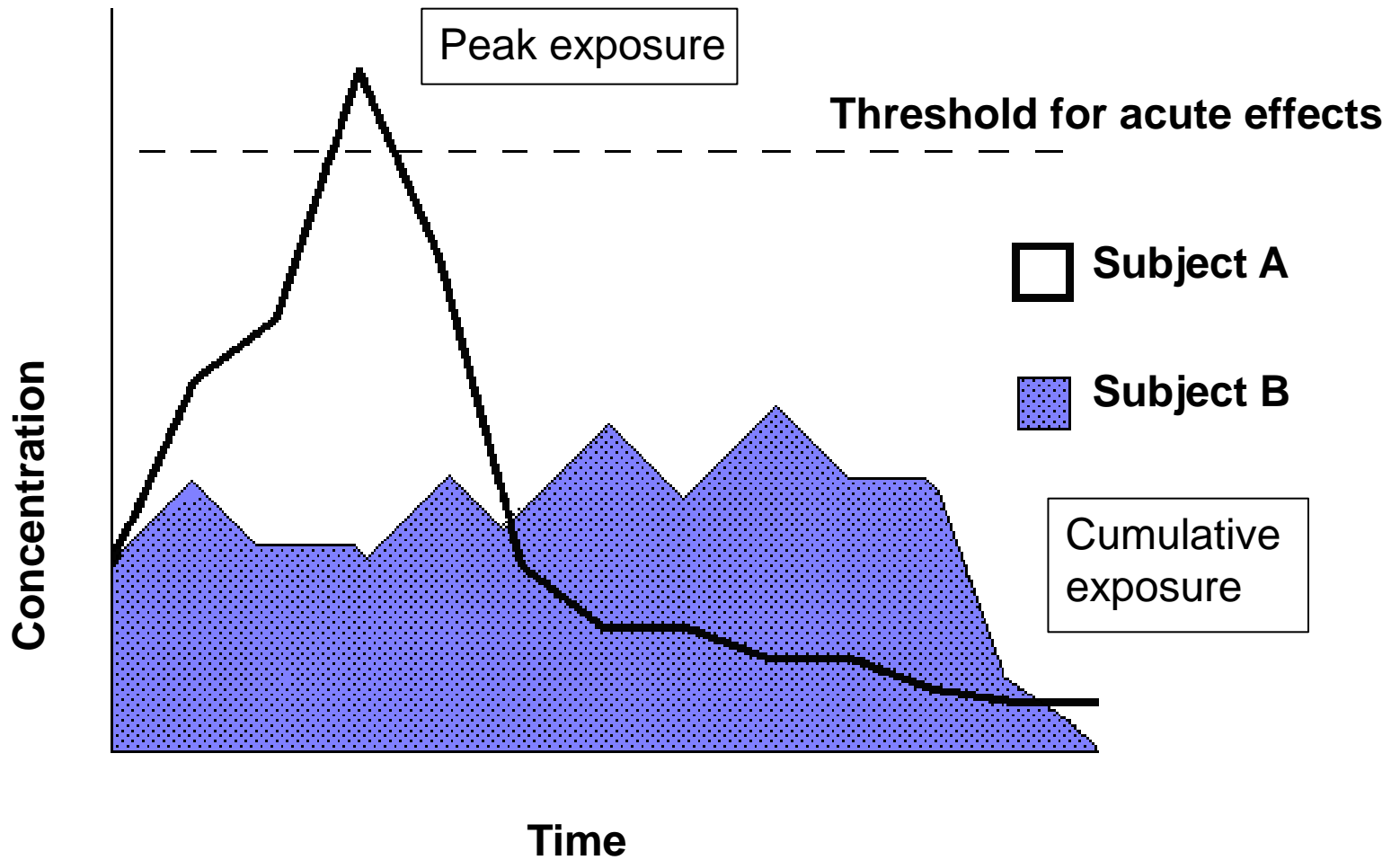
Children



- **Rapid metabolism**
 - Higher consumption of food and water per unit weight
 - Higher inhalation volume per unit weight
- **Development**
 - Immature organ system
 - Immature metabolism
- **Behavior**
 - Hand-to-mouth activity, sucking and biting
 - Live close to the ground



Exposure pattern



”Poor data in → Poor data out”


- Selection of study participants
 - representative sample of the study population
- Sample collection
 - representative samples collected
- Analysis
 - analytical measurement errors
- Information
 - questionnaire data not correct
- Misclassification of exposed/non-exposed
 - Ever exposed/never exposed
- Study population
 - Non-participants are significantly different from the participants
 - Participants change their behaviour and habits during the study

Variability and uncertainty

- Variability
 - True variation of individual data (e.g. standard deviation, variance)
 - Body weight
 - Uncertainty
 - Lack of knowledge about specific factors (e.g. concentration of contaminants)
 - Sampling errors
 - Analytical errors
- The variability cannot be reduced
- but the uncertainty of the variability can be reduced

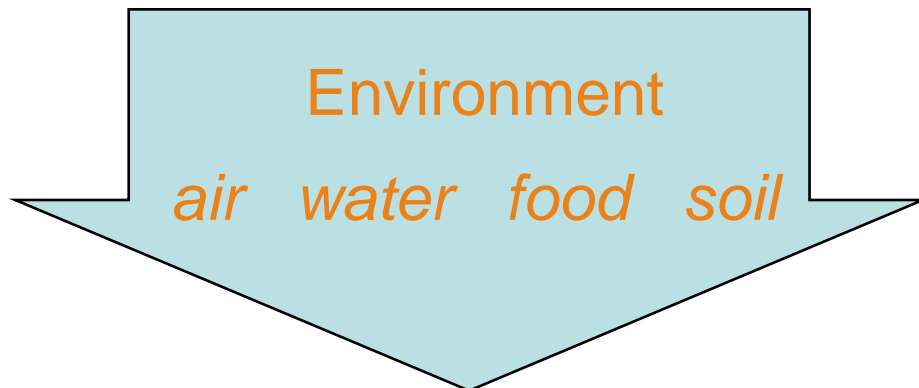
Human Risk Assessment

Risk assessment

- 
- Hazard assessment
 - Exposure assessment

Risk characterization

Exposure pathways



oral inhalation dermal



Risk characterisation

The estimation of the **incidence and severity of the effects likely to occur** due to actual or predicted exposure to a chemical.

The levels of exposure are compared with the threshold levels for each effect.

- Where it is not possible to determine a threshold level for one effect, a qualitative or semi-quantitative approach is used.

Risk Assessment in EU

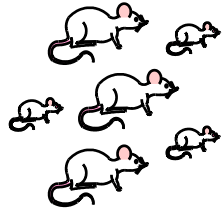
Chemical Safety Assessment (CSA)

- The goal of the CSA is to identify and describe the conditions under which the risks are controlled.
- Risks are regarded as controlled when the estimated exposure levels do not exceed the **derived no effect levels (DNEL)**
- The entity carrying out the CSA needs to document the relevant data, judgements, justifications and conclusions in a **chemicals safety report (CSR)**

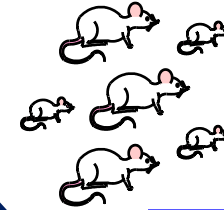
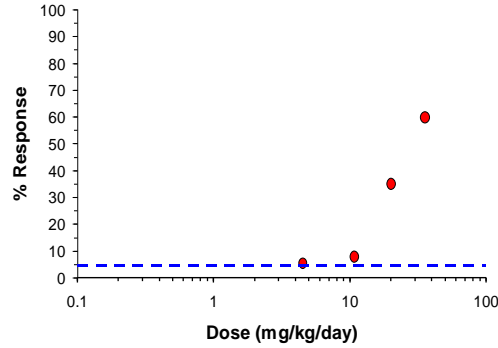
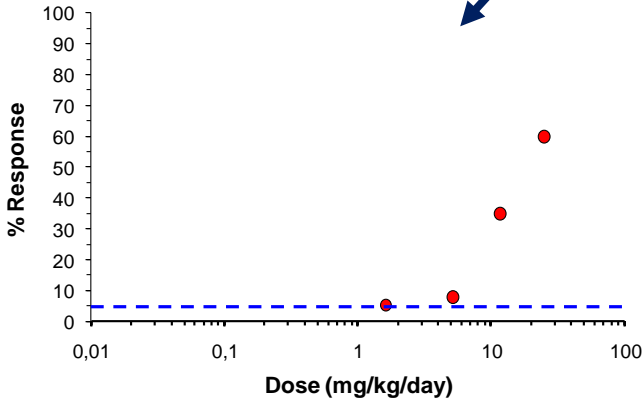
Threshold or non-threshold mode of action

- For the human health end-points a distinction needs to be made between effects by a threshold or a non-threshold mode of action.
- If no-effect levels for human health cannot be determined, the risk characterization is based on semi-quantitative or qualitative assessment of the likelihood that adverse effects are avoided.

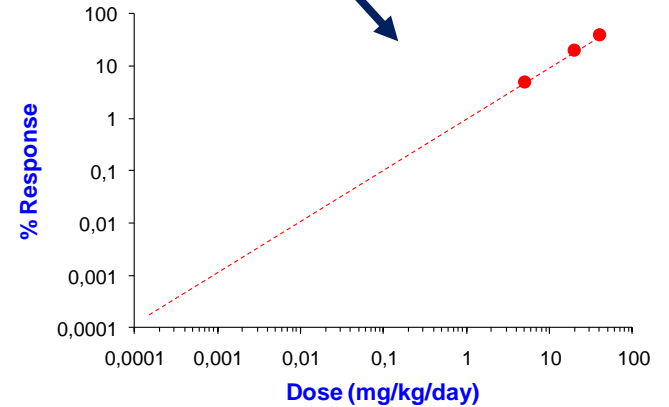
Dose-response in animals



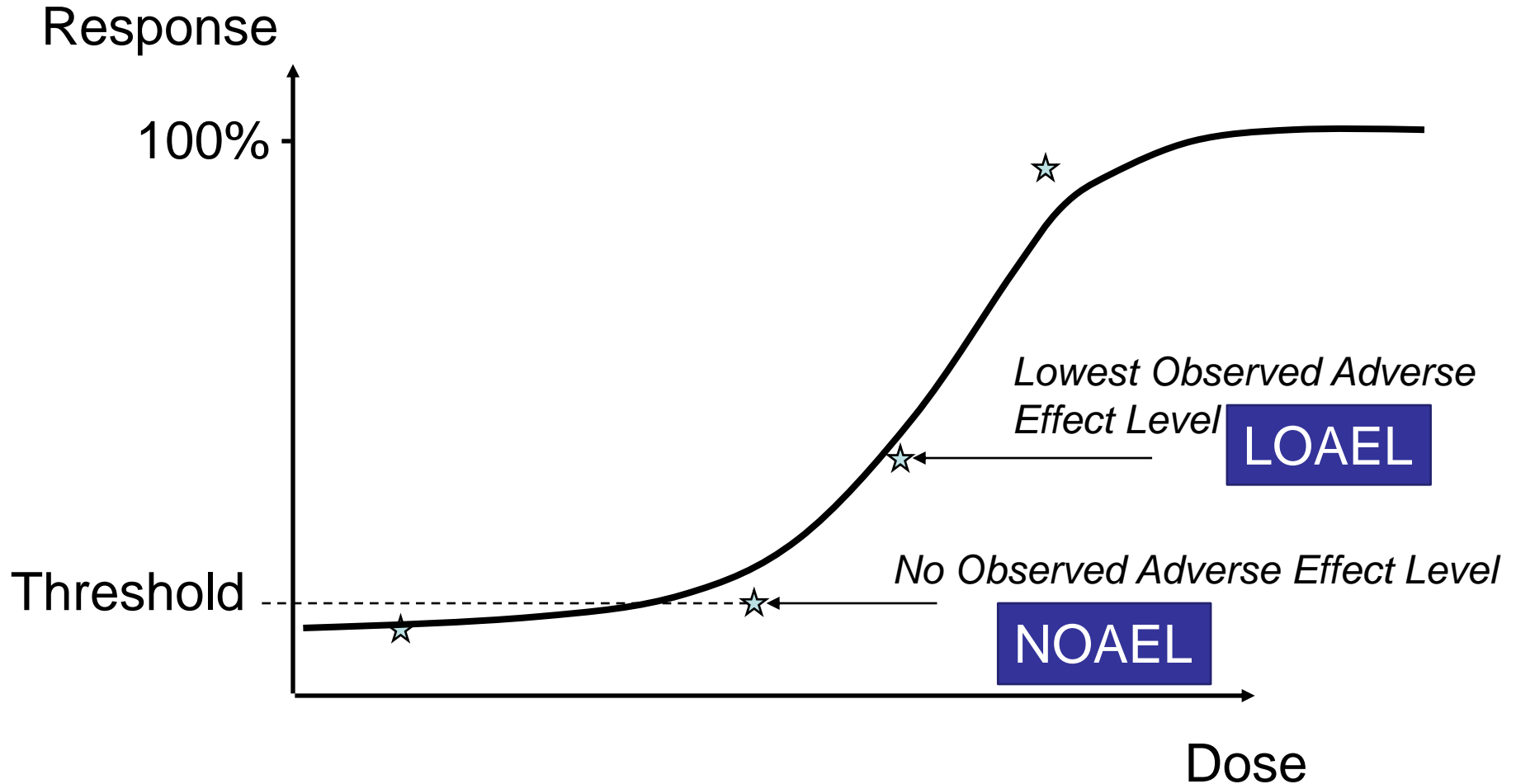
THRESHOLD

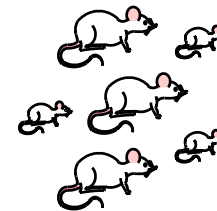
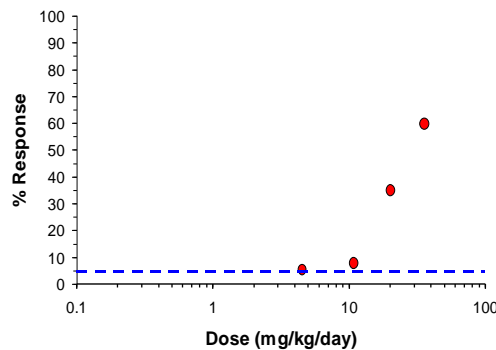
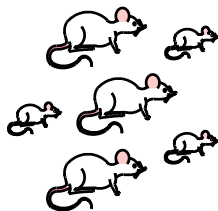


NON-THRESHOLD



Dose-response relationship

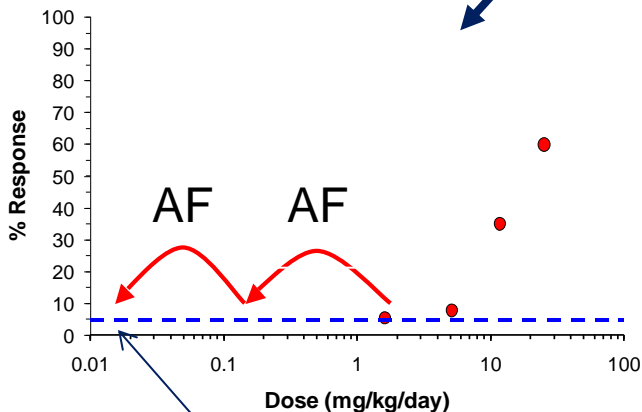




Derived No-Effect Level (DNEL)

the level of exposure to the substance below which no adverse effects are expected to occur.

→ the level of exposure to the substance above which humans should not be exposed



DNEL

AF = Assessment Factor

$$\text{DNEL} = \frac{\text{NOAEL}}{\text{AF} \times \text{AF}}$$

Assessment Factors

- To address the differences between the experimental data and the human situation, taking into account the uncertainties in the extrapolation procedure and in the available data set.
 - Aspects to consider:
 - interspecies differences
 - intraspecies differences
 - differences in duration of exposure
 - issues related to dose-response
 - quality of whole database.
- Often $10 \times 10 = 100$
for inter individual and inter species variation

Risk characterisation ratios (RCRs)

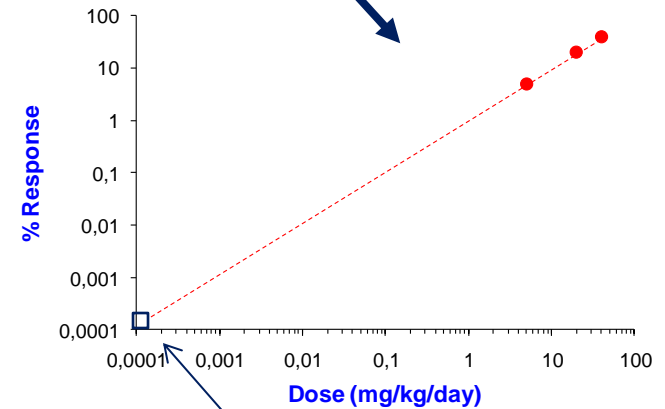
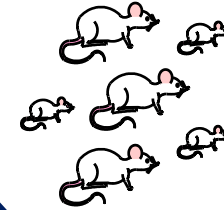
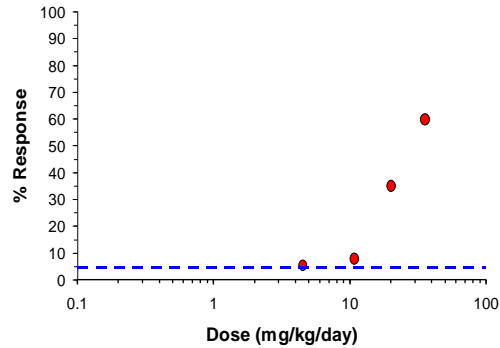
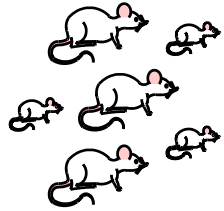
When the leading health effect is a threshold effect with a DNEL:

$$\text{RCR} = \text{Exposure}/\text{DNEL}$$

$\text{RCR} < 1 \rightarrow$ Risk is adequately controlled (Safe use)

$\text{RCR} > 1 \rightarrow$ Risk is NOT controlled

If the risk characterisation shows that **risk is not controlled**, an **iteration** of the CSA is needed



Derived Minimum Effect Level (DMEL)

When the leading health effect is a **non-threshold effect** for which a DMEL has been derived (e.g. for non-threshold carcinogenicity), a semi-quantitative risk characterisation can be conducted

DMEL

Derived Minimum Effect Level (DMEL)

Exposure < DMEL → Exposure is controlled to a *risk level of low concern*

Exposure > DMEL → Risk is NOT controlled

If the risk characterisation shows that **risk is not controlled**, an **iteration** of the CSA is needed

Iterations of the CSA - Strategy

- **Improving the hazard information** - if a limited toxicity data set is available
- **Improving the exposure information** – Iterations on exposure data or on assumptions, refinement of data on substance properties, emission data, exposure assumptions, model definition or complexity, or replace model predictions by measured data.
- **Improving information on operational conditions** - The description of the operational conditions can be refined to get closer to reality
- **Improving information on risk management** - such as on-site waste water treatment, changing to a closed system or improved recirculation of processing chemicals

Risk management measures

- Measures that **control the emission** of a substance **and/or exposure** to it.
 - Any action, use of tool, change of parameter state that is introduced during manufacture or use of a substance in order to **prevent, control, or reduce exposure**

Includes:

- **containment of process (closed system),**
- **waste water treatment,**
- **local exhaust ventilation,**
- **exhaust air filters,**
- **personal protective equipment (gloves etc.), etc.**

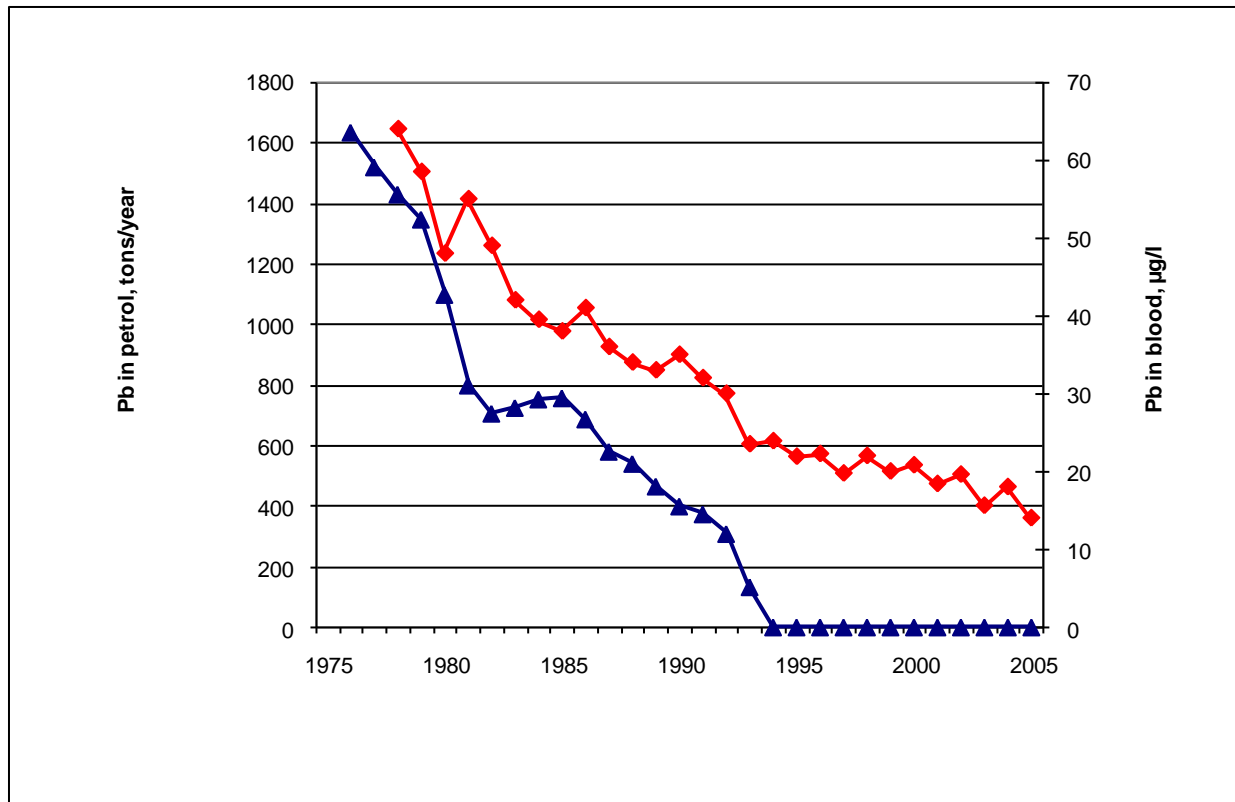
Risk characterisation - Example

NOAEL	1 mg/kg x day
AF	100 (10x10)
DNEL	0,01 mg/kg x day
Exposure media	Drinking water
Concentration	1,5 mg/l
Media contact	2 l/day
Body weight	60 kg
Exposure	$(1,5 \times 2)/60 = 0,05 \text{ mg/kg x day}$
RCR	5

Exposure > DNEL → **risk is not controlled**

Evaluation of risk management banning of lead in gasoline

Lead in
Gasoline
In Sweden

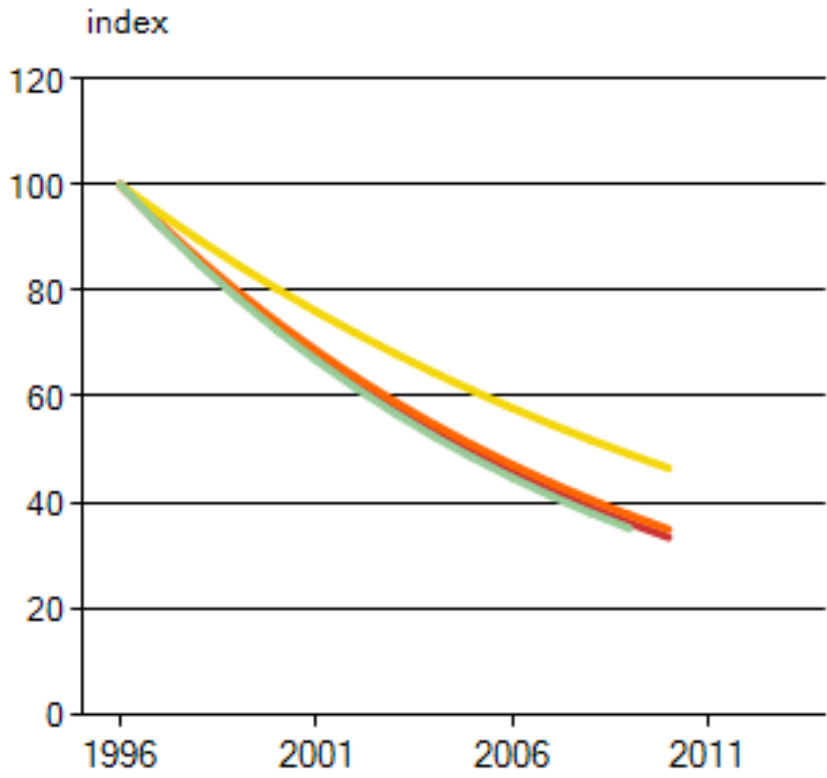


Lead in
blood,
children
3-12 year

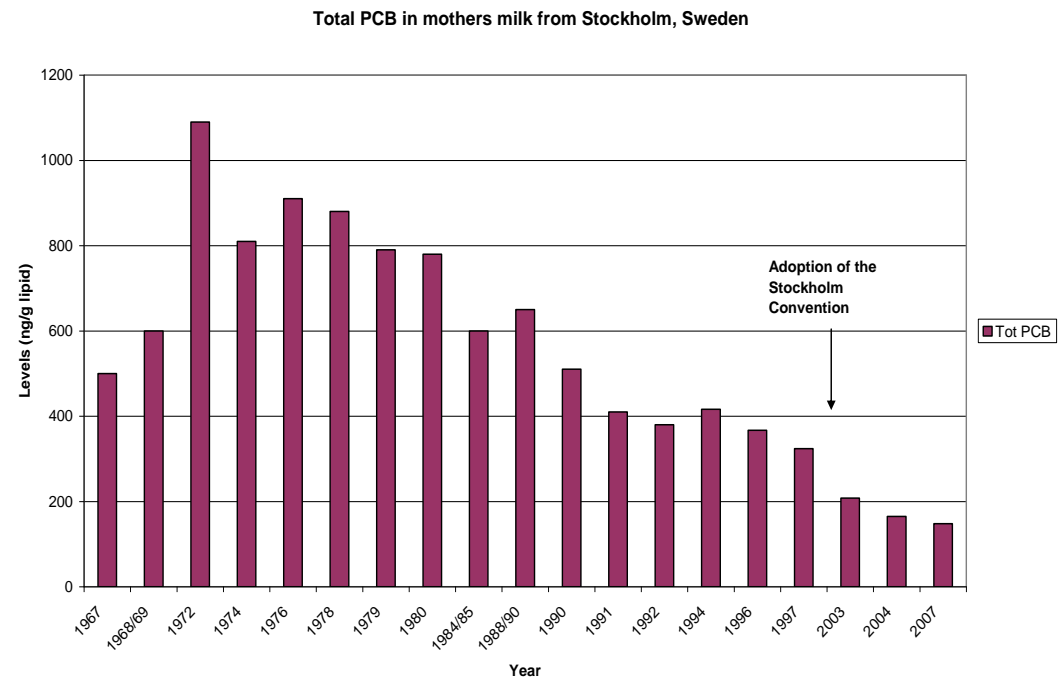
Swedish Health Related Environmental Monitoring Program, 2006

Monitoring status and trend

Pollutants in mother's milk



- PCB 153
- dioxiner
- PBDE (bromerat flamskyddsmedel)
- DDE (nedbrytningsprodukt av DDT)





LUNCHBREAK

Continue at 13:00