foodregsci

Reviewing Hazard Characterization Requirements as Part of Food Chemical Risk Assessment

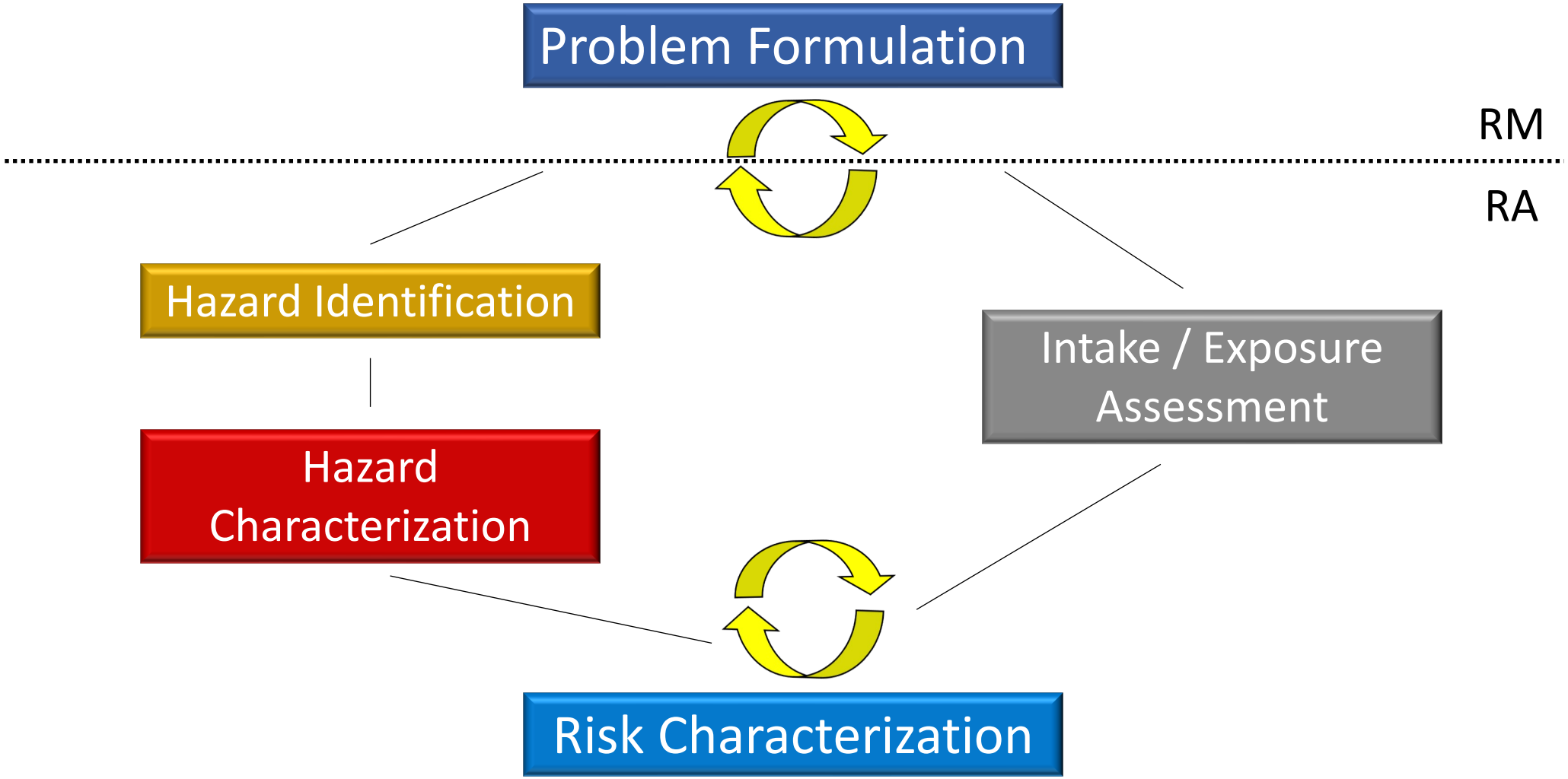
Prof. Samuel Godefroy, Ph.D. *| Full Professor, Food Risk Analysis and Regulatory Policies*

Review of a Risk Assessment Approach…

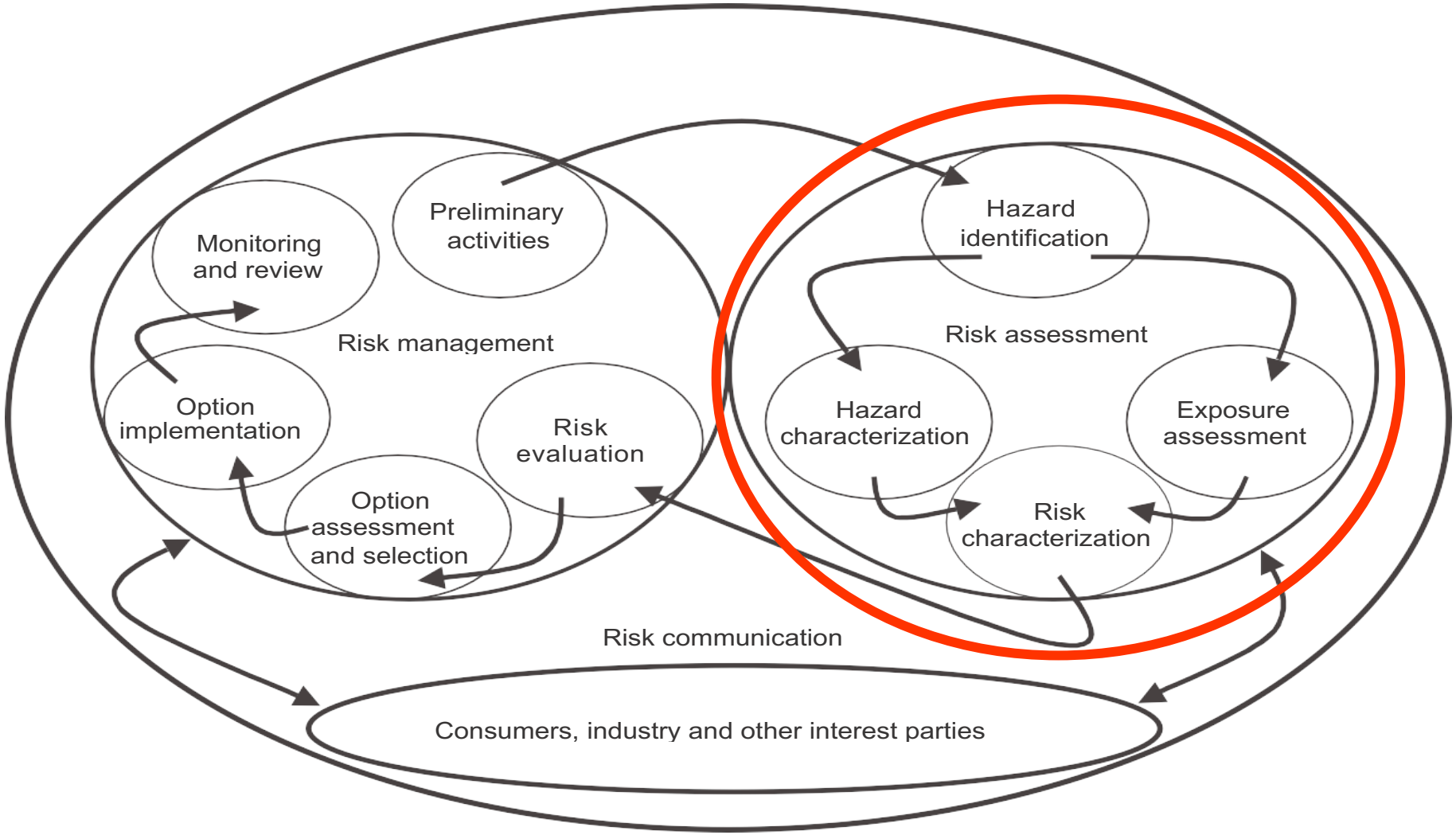
Reviewing the notions of Hazard and Risk

Reviewing the various approaches to achieve hazard characterization for chemicals in food

Risk Assessment Procedure: A Scientific Process



Moving to Scientific Assessment



In the Context of Risk Assessment…

Step 1: Hazard Identification

- ❑ Assess toxicity of chemicals:
  - Does the agent causes adverse effects? (qualitative: yes or no)
- ❑ Which adverse effects?
- ❑ Source of Data :
  - Tests *in vitro*
  - Studies on animals
  - Epidemiological studies

In the Context of Risk Assessment…

Step 2: Hazard characterization

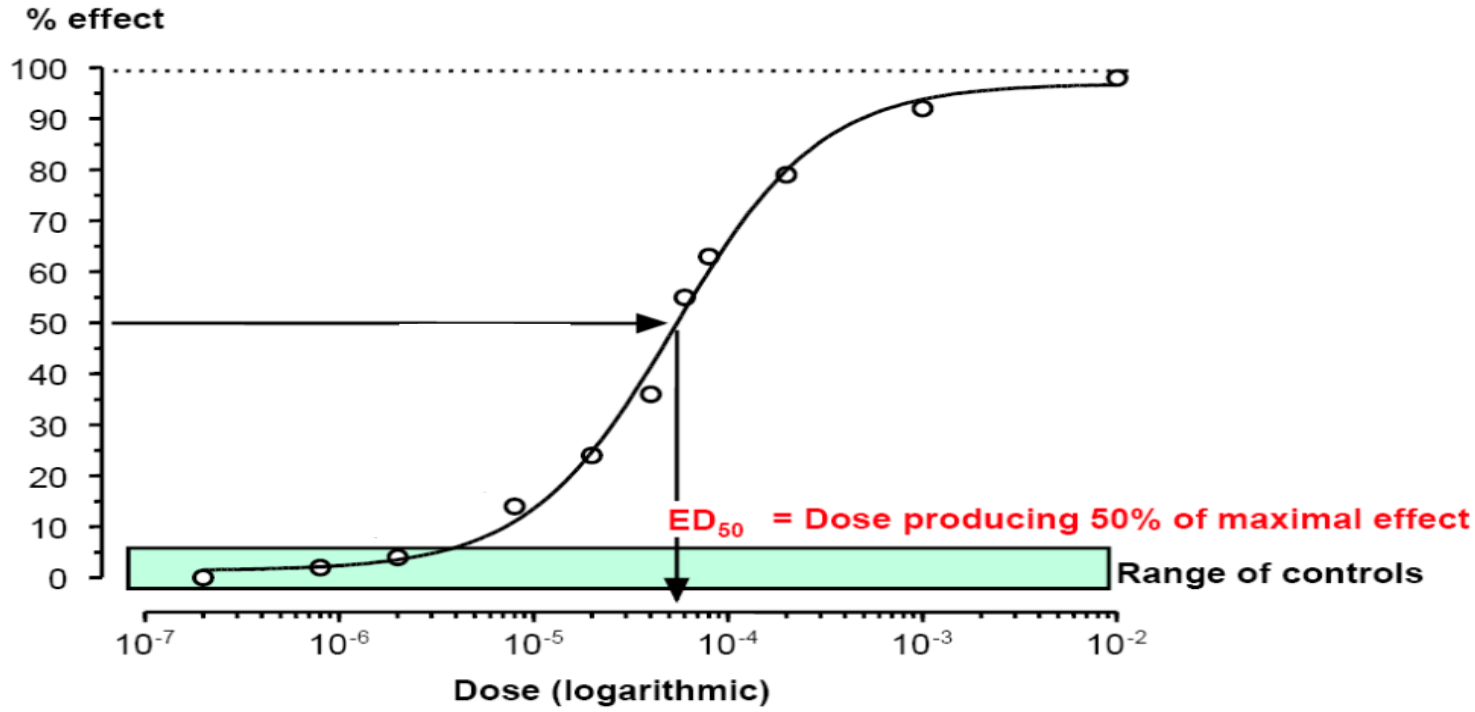
- ❑ Quantitative (+ qualitative) evaluation of the adverse effects

- ❑ Source of Data :
  - Dose-response relations
  - Expected Information:
    - Thresholds : NOAEL, LOAEL,
    - Mechanism of action
    - Individual susceptibility
    - Differences animal-human
    - Differences within the human population (men/women, children / adults)

Risk assessment

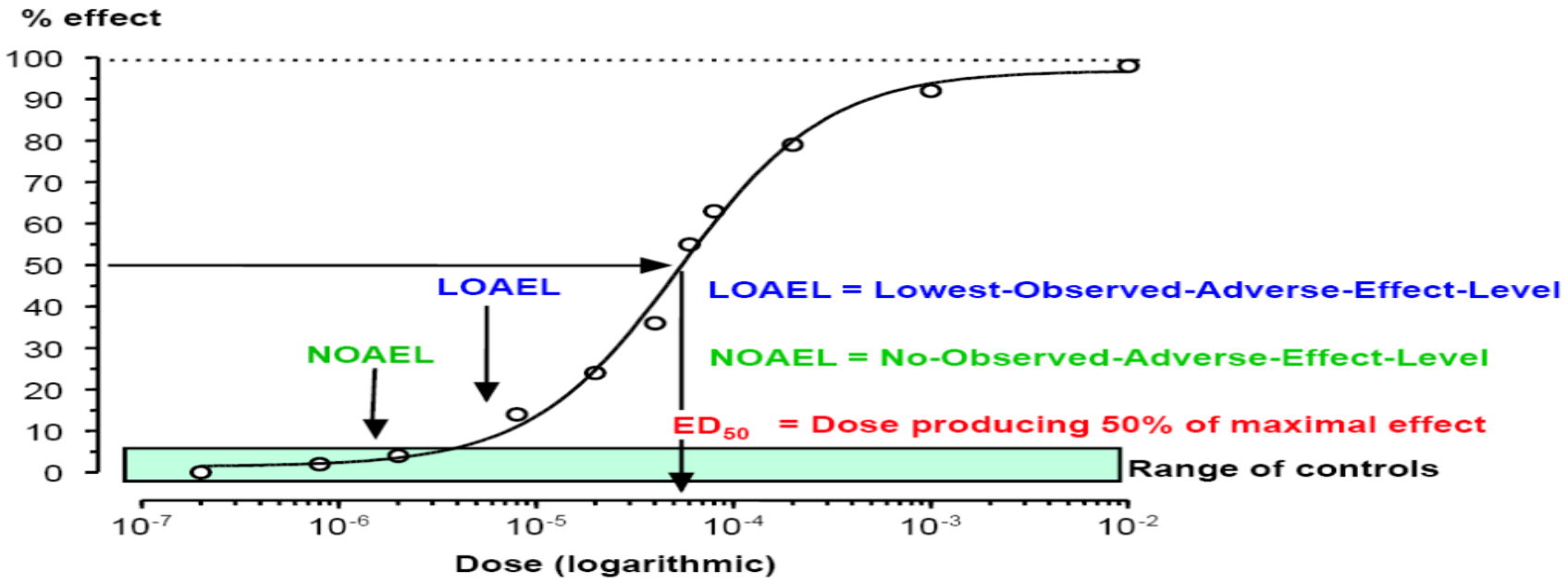
Dose Response Curve and Threshold

- Threshold: is a dose/concentration of a substance, above which the substance starts to produce toxic effects or below which no (significant) toxic effects are observed (= not statistically significantly different from the background)
- With this approach, we define safety (acceptable or low risk) through the dose that is lower than the threshold



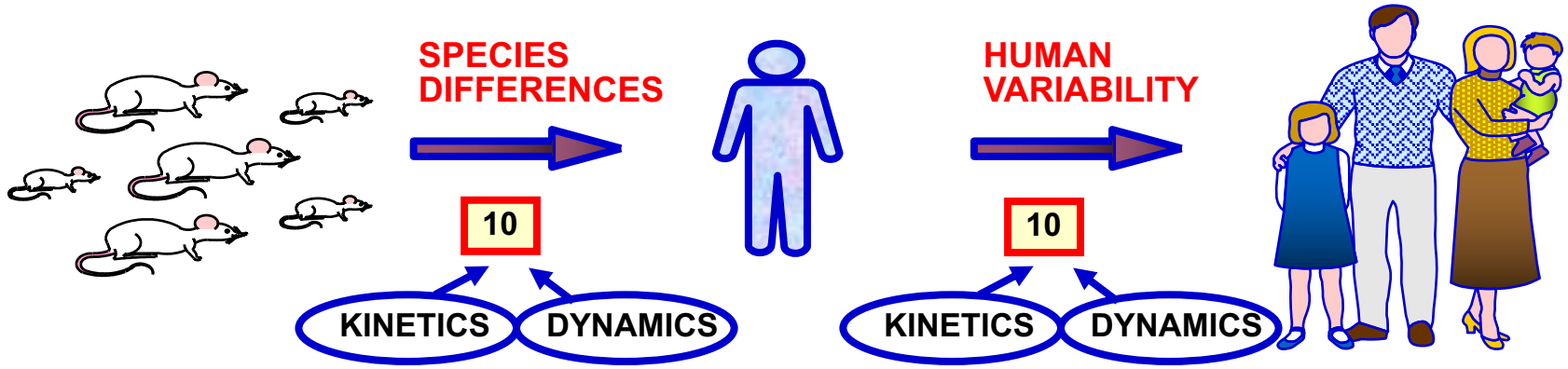
When a Toxicological Threshold Exists : Key Parameters

- **NEL** (no-effect-level), **NOEL** (no-observed-effect-level), **NAEL** (no-adverse-effect-level), **NOAEL** (no-observed-adverse-effect-level)
- **LEL** (lowest-effect-level), **LOEL**, **LOAEL** (lowest-observed-adverse-effect-level)



Default Uncertainty Factors

The usual 100-fold uncertainty factor includes a 10-fold factor for species differences



The 10-fold interspecies factor allows for both toxicokinetics and toxicodynamics

- Uncertainty factor ("safety factor") generally 100
  - 10 for interspecies variation, 10 for human variation

- UF modified if:
  - Derived from human data
  - Inadequacies in the database

Special Considerations: Population Subgroups

Potentially sensitive subgroups include:

- **Pregnant women** – the developing foetus is a vulnerable life stage
- **Neonates** – have both immaturity of elimination processes and developing organ systems
- **Children** – eliminate chemicals more rapidly than adults but have developing body functions
- **The elderly** – have a decreased ability to eliminate chemicals by either metabolism or renal excretion

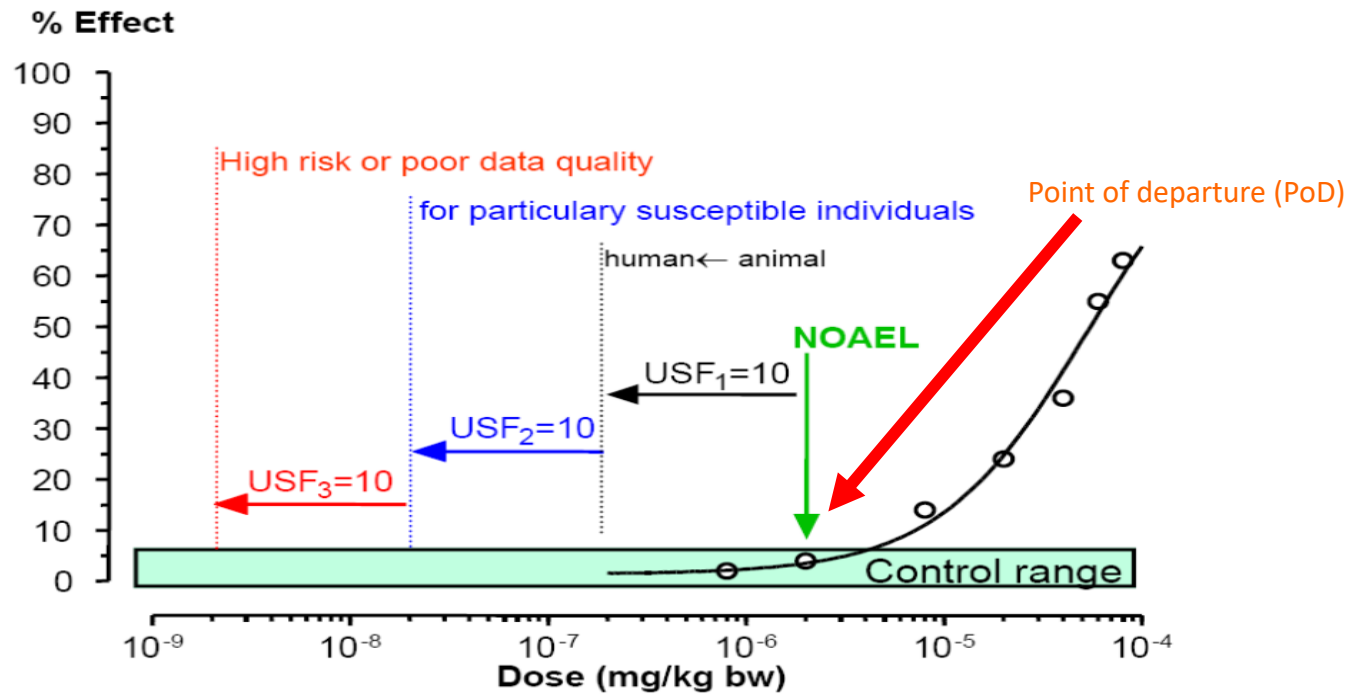
Goal of the RA: protect most sensitive part of the population

- Appropriate animal studies should cover these life-stages

How Do We Account For Uncertainty

NOAEL:

- Highest dose level of a substance used in a test at which no statistically significant adverse effects were observed (in mg/kg bodyweight/day)



ADI and TDI Concept

- Old concept : dating back to 1961 (WHO)
- ADI (acceptable daily intake): used for safety assessments of substances that are deliberately added e.g. food additives
- TDI (tolerable daily intake): used for substances that are not expected to be present (undesired) e.g. food contaminants
- Both values ADI or TDI represent the amount of the substance (additive or contaminant) which can be taken up daily during the whole life (chronic) without appreciable risk according to current knowledge
- This approach works only when a threshold exists (NOEL)
  - Not applicable for genotoxic carcinogens
- 1. Differences between animal and human

  2. Individual variation (children, sick/elder persons, enzymatic polymorphismus)
- Uncertainty factor: USF = 10-100

TDI = NOEL/USF (in mg/kg Bodyweight (BW)/day)


thank you
danke
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ngiyabonga
teşekkür ederim
рахмат
Баярлалаа
спасибо
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감사합니다
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