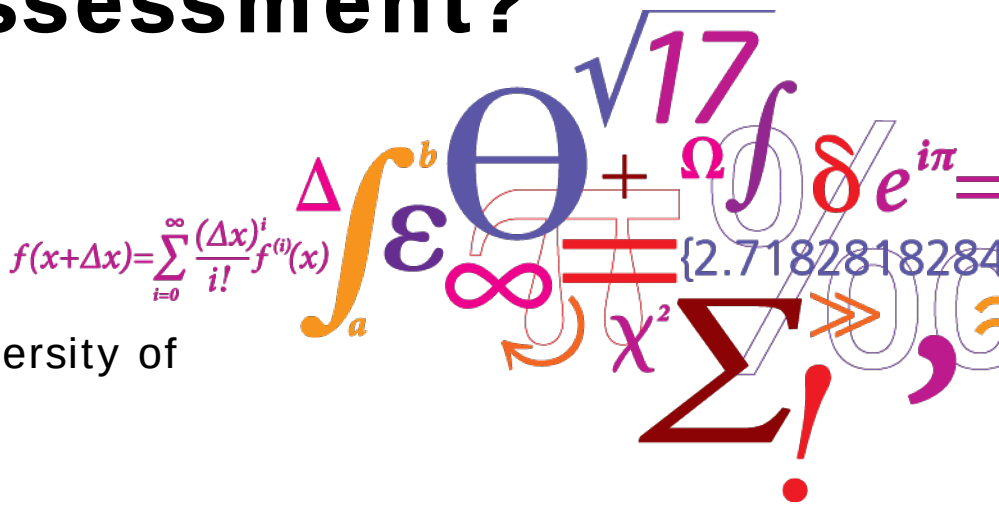
GMASSURE

What is risk assessment?



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Aim of the session

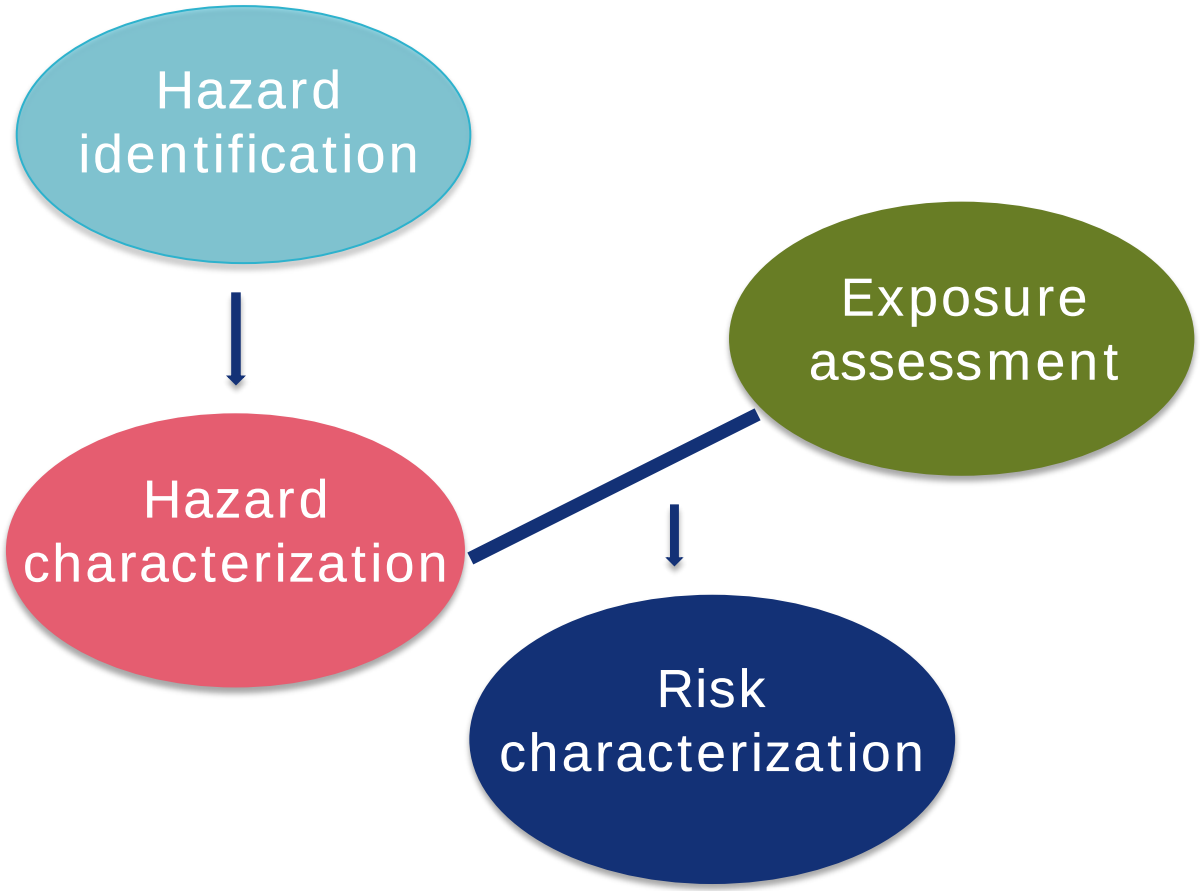
- Understand the basic principles of toxicological risk assessment
- To get an introduction to the different steps in a risk assessment
- Understand the difference between GMO and chemical risk assessment

Why risk assessment

- There are probably different views (consumer vs. Industry)
- Assess the risk - of food
- To realise what we know and what we don't know
- For regulatory purposes

Risk assessment

Risk assessment consists of the following steps



Definition of hazard and risk

Hazard is the inherent property of an agent having the potential to cause adverse effects in an organism exposed to the agent.

Risk is the probability of an adverse effect in an organism caused under specified circumstances by exposure to an agent.

What effect?

At what dose?

How?

What are we exposed to?

What is the probability of effect?

What is the severity of effect?

Toxicokinetics (ADME)

Toxicodynamics (Effects)

Critical effect

Dose response

Concentration (food)?

Intake (food)?

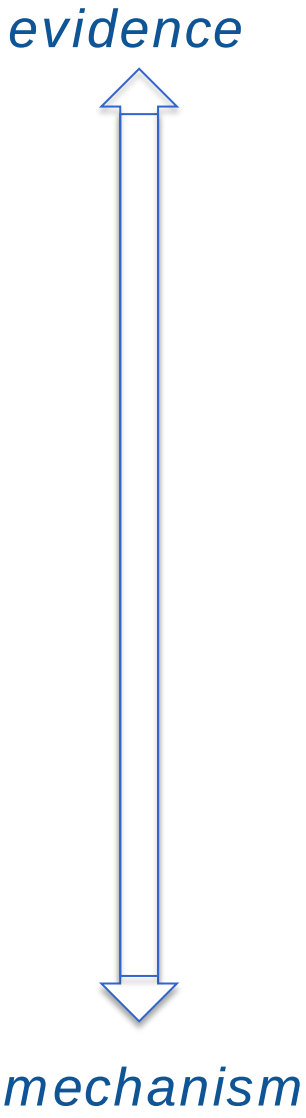
Conclusion on hazard characterisation and exposure assessment

Hazard identification

Identification of the type and nature of adverse health effects that a food or food ingredient has an inherent capacity to cause

Hazard identification

- Human data (case reports, observational studies, intervention trials)
- Studies in experimental animals
- In vitro/cell culture studies
- Structure-activity relationships (SAR)



Toxico kinetics

What the body does to the chemical

- Absoprption
- Distribution
- Metabolism
- Excretion

Also called ADME studies

Toxicodynamics

What the chemical does to the body

Effects:
Change in the morphology, physiology, growth, development, reproduction or life span of an organism

Adverse effects:

- Impairment of functional capacity
- Impairment of the capacity to compensate for additional stress
- Increase in susceptibility to other influences

Hazard Characterisation

Quantification, dose-response relationship, vulnerable subgroups, uncertainties

Hazard Characterisation

Identify the critical effect (mg/ kg bw/day)

One definition of critical effect(s) is:

The adverse effect(s) which occur at the lowest dose. It may or may not be the most severe effect.

Critical effect could be a local as well as a systemic effect

Identification of Critical effect

Human data: Epidemiological data

Animal experiments: Dose response studies

Whether data from animal experiments or human data are used is a case by case decision

Dose response relationship: No Observed Effect Level (NOAEL), Benchmark dose modeling

The no-observed-adverse-effect Level (NOAEL)

The highest level where the critical effect is **not** seen

The ”no observed adverse effect level” (NOAEL) is determined from the most sensitive study in the most sensitive species tested (if relevant for humans)

What if no critical effect(s) are seen?

The NOAEL is then the highest level tested in the human/animal study

Exposure assessment

The aim is to obtain a realistic estimate of total human exposure of an agent.

Concentrations in food item(s) * occurrence in food item(s)

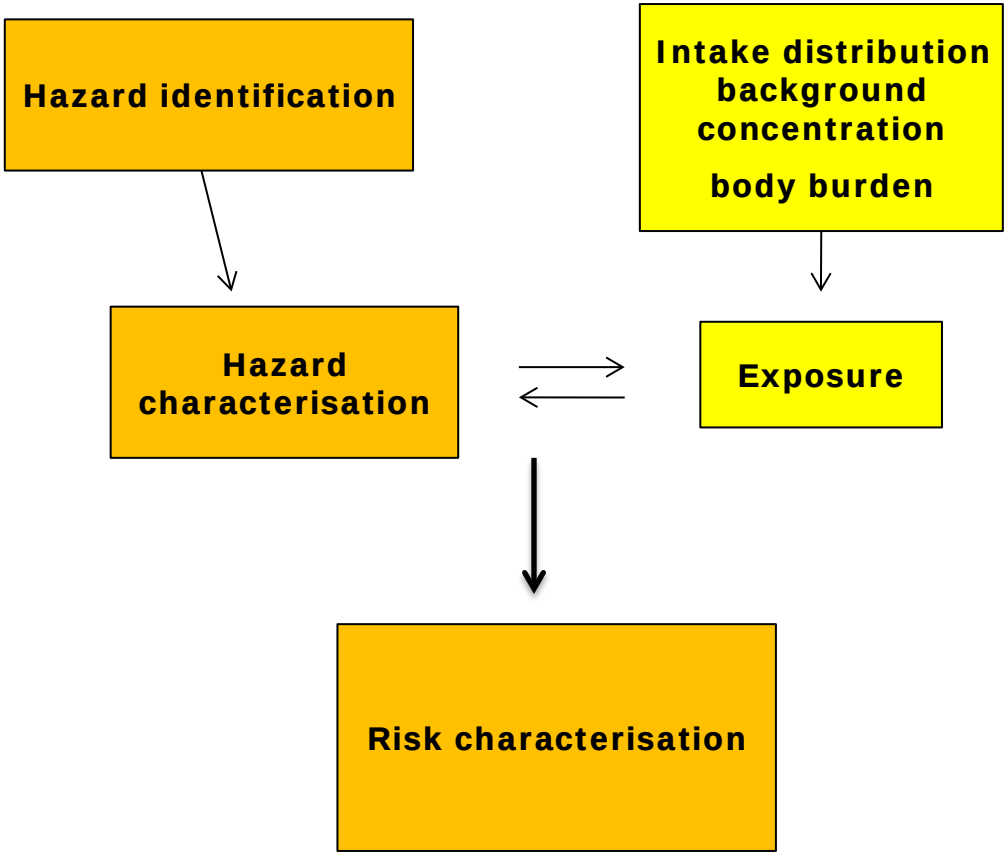
For each food item concentration in the food item * by the occurrence of the food item

The total exposure is the sum of the exposure of all the food items

Risk characterisation

Risk characterisation is the stage of risk assessment that integrates information from exposure assessment and hazard characterisation into advice suitable for use in decision-making

The Risk Assessment



What kind of information could be relevant for the risk assesment

The analytical/compositional characteristics

Nutritional characteristics

The predicted exposure of the food/chemical

What kind of safety investigations could be relevant for the risk assessment

In vitro studies (genotoxicity)

Animal studies (ADME, 28-, and 90-day studies)

Studies in humans

Post-launch monitoring

You have performed a risk assessment of GMO XX17

A journalist calls you asking whether you now can guarantee that there will no risk to the consumer

Your answer will be: ?

Where in the risk assessment procedure could uncertainties be identified?

Risk Assessment Chemical vs. GMO

Chemicals:

- Observed toxicity
- Dose-response
- Low intake
- Part of food
- Absolute assessment

GMO:

- Neglegible toxicity
- No dose-response
- Medium-high intake
- Whole food
- Comparative assessment

The Risk Assessment of GMOs

A comparative assessment

What about controls?

Key Elements for the assessments of GMOs

Molecular characterization of the genetic modification event

Characterization of donor and host organism

- Methods
- Inserted genes
- Gene expression

Analysis of agronomical and compositional proprieties

Key Elements for Assessments of GMOs

Toxicity/allergenicity/nutritional testing

Post market monitoring

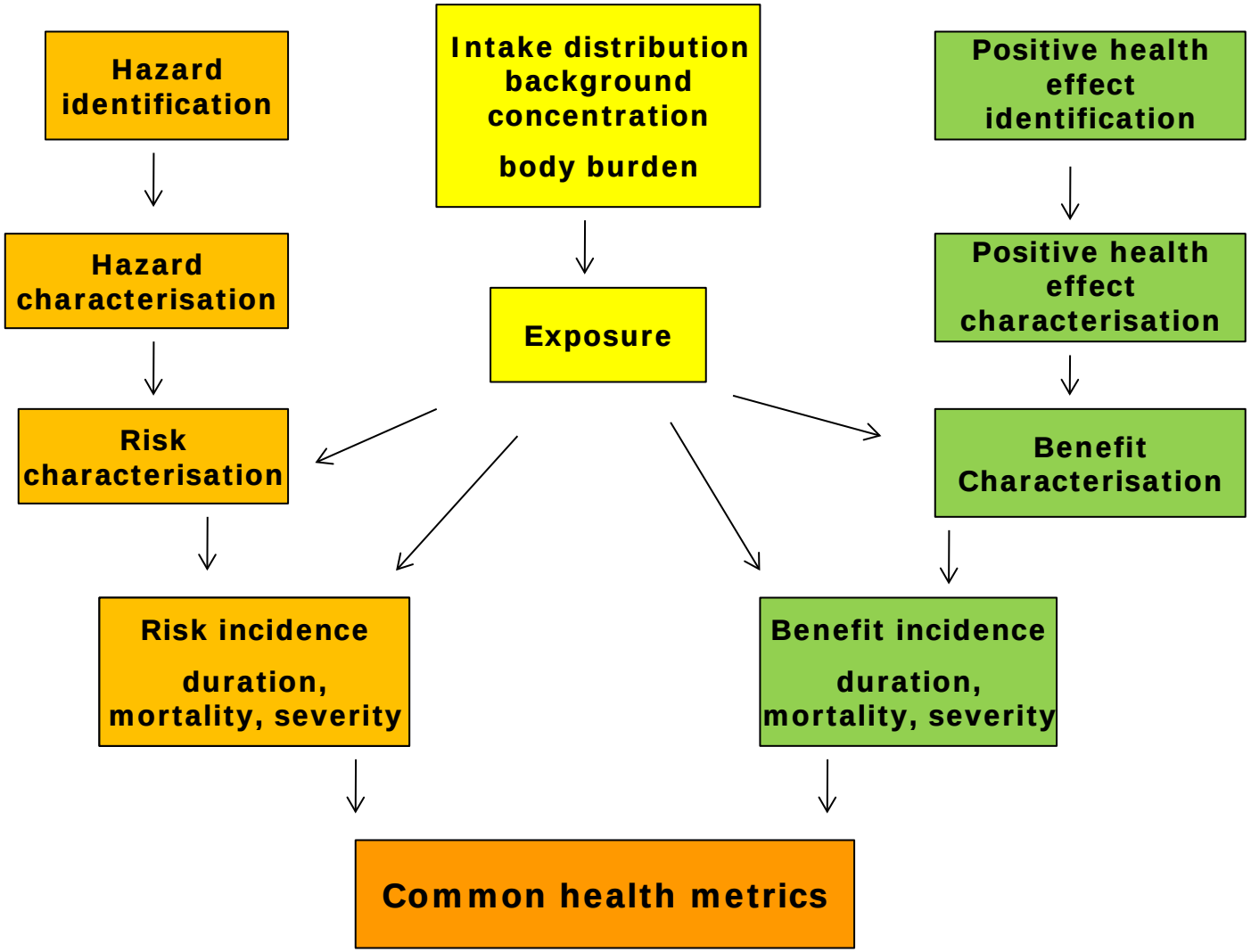
Environmental risk assessment

Environmental monitoring /surveillance

What about the benefit of GMOs?

Not part of the risk assessment

Method for a risk-benefit assessment exists!


Hazard identification
Intake distribution background concentration body burden
Positive health effect identification
Hazard characterisation
Exposure
Positive health effect characterisation
Risk characterisation
Benefit Characterisation
Risk incidence duration, mortality, severity
Benefit incidence duration, mortality, severity
Common health metrics

Thank you

Questions?