Risk Assessment for Regulatory Purposes

Katrina Campbell
Professor in Food Security & Diagnostics

E-mail: katrina.campbell@qub.ac.uk

Risk analysis

Learning Outcomes

- To define risk analysis and assessment
- To define each of the 4 basic steps of a risk assessment
- To provide examples of some factors that affect risk perception and risk analysis
- To define voluntary vs. involuntary risk
- To explain key differences between microbial and chemical risk assessment

Risk analysis for food safety

- Risk analysis is widely recognised as the fundamental methodology underlying the development of food safety standards.

- The WHO and the FAO are in the forefront of the development of risk-based approaches for the management of public health hazards in food.

- The approach used is called risk analysis:
  - risk assessment
  - risk management
  - risk communication

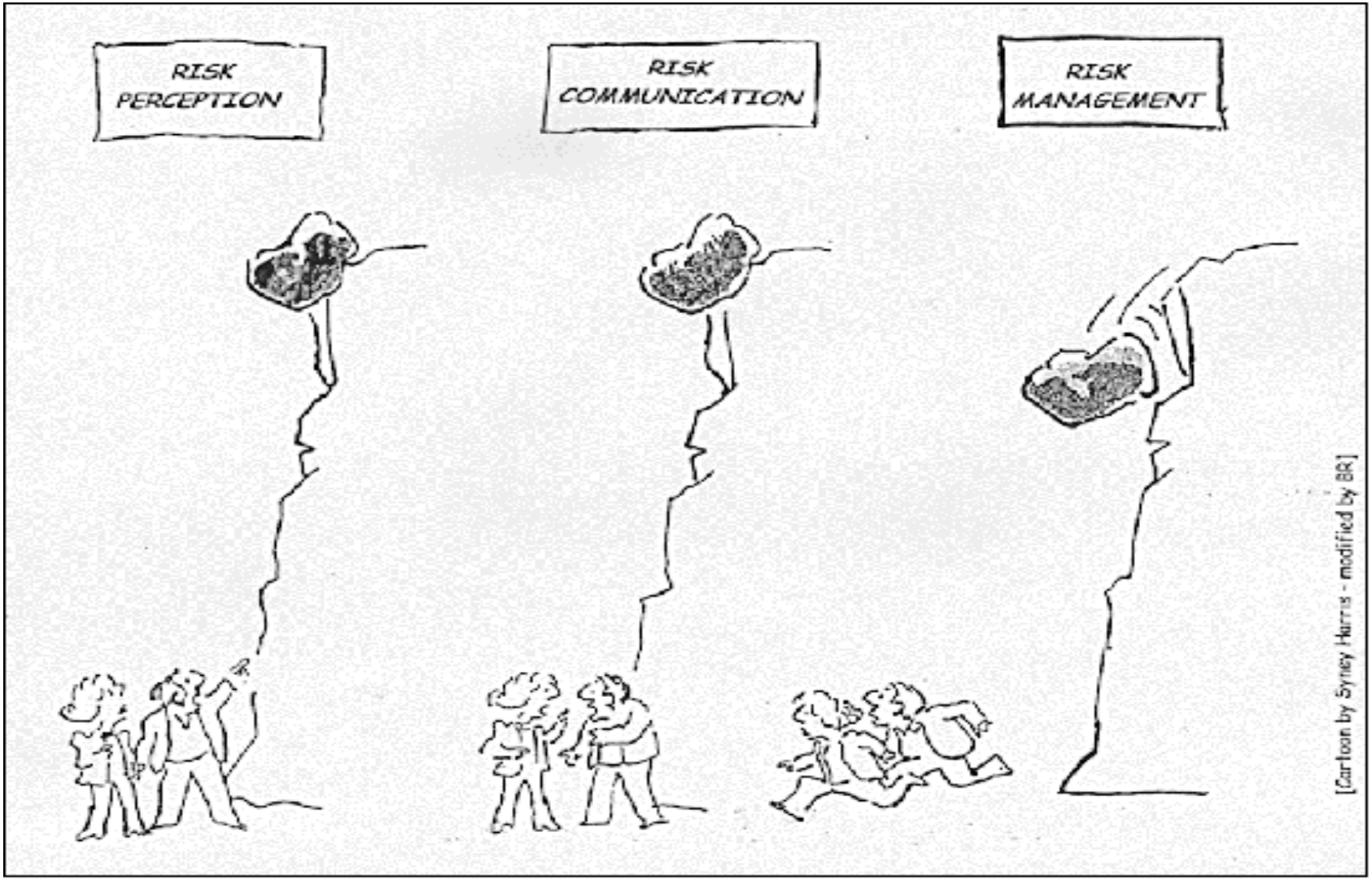
What is risk?

A controversial but inherent property of everyday life

Risk	Lifetime risk of mortality
Cancer from cigarette smoking (one pack per day)	1:4
Death in a motor vehicle accident	2:100
Homicide	1:100
Home accident deaths	1:100
Cancer from exposure to radon in homes	3:1000
Death from hepatitis A	3:1000
Exposure to aflatoxin in peanut butter	6:10,000
Diarrhea from rotavirus	1:10,000
Exposure to typical EPA maximum chemical contaminant levels	1:10,000–1:10,000,000

Even though risk may be relatively low (1:10,000,000) how does one decide what is acceptable risk? A number of factors that affect risk perception and risk analysis:

Factor	Conditions associated with increased public concern	Conditions associated with decreased public concern
Catastrophic potential	Fatalities and injuries grouped in time & space	Fatalities and injuries scattered & random
Familiarity	Unfamiliar	Familiar
Understanding	Mechanisms or process not understood	Mechanisms or process understood
Controllability (personal)	Uncontrollable	Controllable
Voluntariness of exposure	Involuntary	Voluntary
Effects on children	Children specifically at risk	Children not specifically at risk
Effects manifestation	Delayed effects	Immediate effects
Effects on future generations	Risk to future generations	No risk to future generations
Victim identity	Identifiable victims	Statistical victims
Dread	Effects dreaded	Effects not dreaded
Trust in institutions	Lack of trust in responsible institutions	Trust in responsible institutions
Media attention	Much media attention	Little media attention
Accident history	Major and sometimes minor accidents	No major or minor accidents
Equity	Inequitable distribution of risks and benefits	Equitable distribution of risks and benefits
Benefits	Unclear benefits	Clear benefits
Reversibility	Effects irreversible	Effects reversible
Origin	Caused by human actions or failures	Caused by acts of nature


RISK PERCEPTION
RISK COMMUNICATION
RISK MANAGEMENT
[Cartoon by Syney Harris - modified by BR]

WHO/FAO approach to risk analysis

Why do we need risk assessment?

- Standards for levels of toxic chemicals or pathogenic microorganisms in water or food
- Analyses of contaminated sites to determine the need for action and the extent of cleanup
- Constructing “what-if” scenarios to compare treatment alternatives and to set priorities for corrective action.
- Evaluating existing vs. new technologies
- Articulating community public health concerns
- Developing consistent public health expectations among different localities

RISK ASSESSMENT

Microbial vs. chemical risk assessment

There are some inherent differences between microbial and chemical risk assessments. Usually disease due to chemical exposure is cumulative over a long period of exposure. In contrast, for microbes, disease may occur following exposure to a single pathogen and will depend on the virulence of the pathogen and the susceptibility of the host. Therefore, one must estimate a risk of infection based on different factors.

Voluntary vs. involuntary risk

Voluntary risk (e.g., puffer fish) is always more acceptable than involuntary risk (e.g., consuming hamburger contaminated with *E. coli*).

It is generally agreed that a lifetime involuntary risk on the order of 1:1,000,000 is small enough to be acceptable or is a tolerable risk.

RISK ASSESSMENT

Definition: The process of estimating both the probability that an event will occur and the probable magnitude of its adverse effects over a specified time period.

Food Safety Risk assessment is:

"the scientific evaluation of known or potential adverse health effects resulting from human exposure to foodborne hazards."

Both chemical and microbial risk assessments can be performed.

Each consists of four basic steps:

1) Hazard identification - identify the chemical (e.g, arsenic) or microbe (e.g, salmonella)

2) Exposure assessment

3) Dose-response assessment

4) Risk characterization

Step 2 - Exposure assessment

The process of measuring or estimating the intensity, frequency and duration of human exposures to a chemical or microbe

Exposure pathway – the path from a source to the receptor

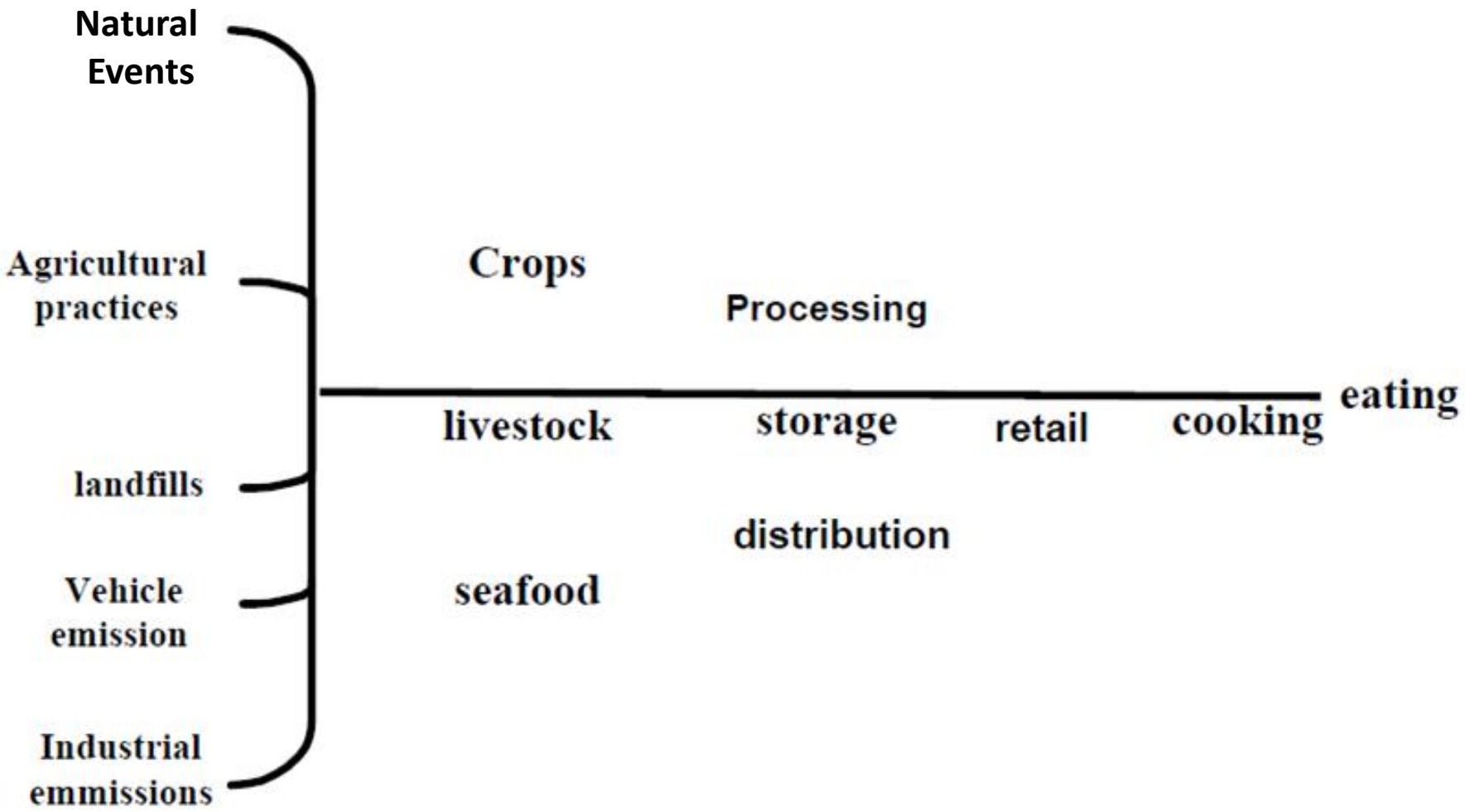
Exposure route – intake pathway

- ingestion

Exposure response is mediated by

- concentration of chemical/microbe
- exposure rate (magnitude, frequency, duration)
- receptor characteristics (body weight, genetics, immunity)

Sources for chemical hazards in the food supply chain



Step 3 - Dose-response assessment

Quantitating adverse effects from exposure based on the degree of exposure

The goal of a dose-response assessment is to obtain a mathematical relationship between the amount of a toxicant/microbe involved in an exposure to the risk of an adverse outcome.

To determine the capacity of an agent to cause harm, we need to quantify toxicity or infectivity.

Dose – mg chemical/body weight
microbes/exposure

Possible responses

- no response
- temporary response
- permanent response
- chronic functional impairment
- death

Step 4 - Risk characterization

Estimating the potential impact of a contaminants based on the severity of its effects and the amount of exposure.

If one looks at the four steps of risk assessment, there is uncertainty associated with each step of the assessment. The various sources of uncertainty include:

- extrapolation from high to low doses
- extrapolation from animal to human responses
- extrapolation from one route of exposure to another
- limitations of analytical methods
- estimates of exposure

In addition, one must consider vulnerable populations that may be impacted differently than the general population by the outcome of a risk analysis.

Uncertainty can be assessed using

- sensitivity analysis – the uncertain quantities of each parameter are varied to find out how changes affect the final risk estimate.

- Monte Carlo simulation – assumes that all parameters are random or uncertain. The computer chooses random variations of the parameters and generates risk estimates.

The final phase of risk assessment is to integrate exposure and dose-response assessments to yield probabilities of effects. Risk analysis can be quite accurate but most risk analysis is associated with a great deal of uncertainty.

Comparison of outbreak data to model predictions for assessment of risks associated with exposure to *Salmonella*

Food	Dose CFU	Amount consumed	Affected rate (%)	Predicted P (%)
Water	17	1 liter	12	12
Pancretin	200	7 doses	100	77
Ice cream	102	1 portion	52	54
Cheese	100-500	28 g	28-36	53-98
Cheese	10^5	100 g	100	>99.99
Ham	10^6	50-100 g	100	>99.99

Risk assessment provides an effective framework for determining the relative urgency of problems and the allocation of resources to reduce risks.

Food safety agencies use risk assessment in a variety of situations:

- Setting standards for chemical or pathogens in water/food
- Assessing risk from GEMS (genetically engineered microbes)
- Conducting baseline analysis of contaminated sites to determine need for cleanup
- Cost/benefit analysis
- Development of cleanup goals
- Constructing “what if” scenarios
- Evaluation of existing and new technologies for pollution prevention and control
- Articulation of public health concerns

What is the role of the WHO in risk assessment?

- WHO provides assessments of chemical and microbiological risk in food to Codex and to Member States.

- The Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) are recognized as being at the forefront of scientific knowledge in assessing the risks of chemicals in food.

- WHO plays a leading role in promoting the collection, collation and evaluation of data on chemicals in foods and the total diet at regional and international levels.

EU Legislation

- EC regulation 315/93 concerns contaminants in food.
- Contaminant = any substance not intentionally added to food.
- Food containing a contaminant in an amount which is unacceptable for public health reasons shall not be placed on the market.
- Contaminants should be kept as low as reasonably possible by following good practices.
- Where necessary, maximum limits are set for specific contaminants in Regulation 1881/2006 and its amendments.

Prevention and Regulation

- “prevention is better than cure” to protect the consumer (humans and animals) from the toxic effect of contaminants
- need for encouraging preventive actions such as good agricultural practice, good storage conditions, use of improved sorting procedures, good manufacturing practice …
- Fixing maximum limits is not contrary to prevention.
- Fixing maximum levels at a reasonably achievable level, stimulates preventive actions and approaches at all stages to avoid contamination of the feed/food chain.
- Regulatory standards (maximum levels) provide a benchmark against the effectiveness of the successful implementation of prevention programmes and provide a tool for control authorities to control the correct application of prevention measures by each actor in the chain

Risk Management

Module co-ordinator: Katrina Campbell
E-mail: katrina.campbell@qub.ac.uk

Risk management

- Risk management is defined within the Codex as

"the process of weighing policy alternatives to accept, minimize or reduce assessed risks & to select & implement appropriate options."

- The four components of risk management frameworks are:
  - Preliminary risk management activities
  - Evaluation of risk management options
  - Implementation of the risk management decision
  - Monitoring and review

Why is risk management essential?

- The outcome of the risk management process is the development of standards, guidelines and other recommendations for food safety.
- Different management decisions may be made according to different criteria and different ranges of risk management options.
- Risk managers, in developing approaches to managing risk, utilise the risk characterization that results from the risk assessment process.

Risk management for contaminants in food

- Scientific risk assessment:
  - assessment of the risks related to the presence of a contaminant in foodstuffs for human health / establishment of a tolerable intake / health based guidance value
  - exposure assessment: human exposure (average and 95 percentile) Particular attention to vulnerable groups of population, high level consumers, ...
  - Risk characterisation: human exposure assessed in relation to the health based guidance value

--> is the basis for the measures to be taken

Risk management for contaminants in food

- Determination of foods/food groups significantly contributing to the exposure
- Occurrence data of the contaminant in the various food/food groups
- Setting a maximum level following the ALARA principle (As Low As Reasonably Achievable). The degree of severity of the application of this principle depends on the relation exposure - tolerable intake
- Other appropriate management tools – e.g. sorting or processing

Risk management tools used for contaminants food

- **Maximum levels**: aflatoxins, ochratoxin A, lead, cadmium, 3-MCPD, nitrates, inorganic tin
- **Maximum levels with regional derogations**: dioxins and dioxin-like PCBs
- **Maximum levels combined with code of practice for prevention and reduction:** patulin, Fusarium-toxins
- **Comprehensive strategy (feed and food) comprising of a combination of maximum levels, action levels, target levels and source-directed measures:** dioxins and dioxin-like PCBs

Risk management tools used for contaminants in food

- **Maximum levels with data collection:** PAH, dioxins
- **Maximum levels combined with dietary advice:** mercury
- **Code of practice:** ethylcarbamate
- **Dietary advice**
- **Data collection**: acrylamide, furan
- **Tools for reduction of presence**: acrylamide combined with monitoring to assess the effective implementation of tools

Risk communication

- Risk communication is “an interactive process of exchange of information and opinion on risk among risk assessors, risk managers, and other interested parties.”

- Risk communication is an integral and on going part of the risk analysis exercise . It makes stakeholders aware of the process at each stage of the Risk Assessment.

Summary: risk analysis framework

Regulatory Limits

Module co-ordinator: Katrina Campbell
E-mail: katrina.campbell@qub.ac.uk

Regulatory limits

- FAO and WHO supported body – Codex Alimentarius Commission – aims to facilitate world trade and protect consumer health by development of international standards for food and feed.
- Outputs include:
- Setting **Maximum Limits for contaminants**
- Publishing **Codes of Practice to reduce contaminants.**

Regulatory limits

- A regulatory limit is otherwise known as a safety limit.
- Regulatory limits are designed to protect the consumers from potential harm and are often set well below the point of danger from being accidentally reached.
- Regulatory limits are established following the process of risk assessment.

Regulatory limits for food contaminants

- A food contaminant is a substance not intentionally added to food but may be present in such food as a result of manufacturing, processing, preparation, treatment, packing, packaging, transport or holding of such food, or as a result of environmental contamination.

- Contaminant levels shall be kept as low as reasonably achievable following good practices.

- Risk analysis involves assessing the risks posed to human and animal health for establishing tolerable daily intakes for various contaminants and setting maximum residue levels (MRLs) for certain contaminants in order to protect public health.

How are regulatory limits determined?

- The amount of exposure to any given agent is identified, above which causes a health effect to be observed.

- The resulting number is divided by a safety factor to ensure that consumers are never exposed to dangerous levels.

Corn contaminated with Mycotoxins

Mycotoxins for breakfast?

Deoxynivalenol
Zearalenone
Ochratoxin A

Ochratoxin A

Aflatoxin M_1

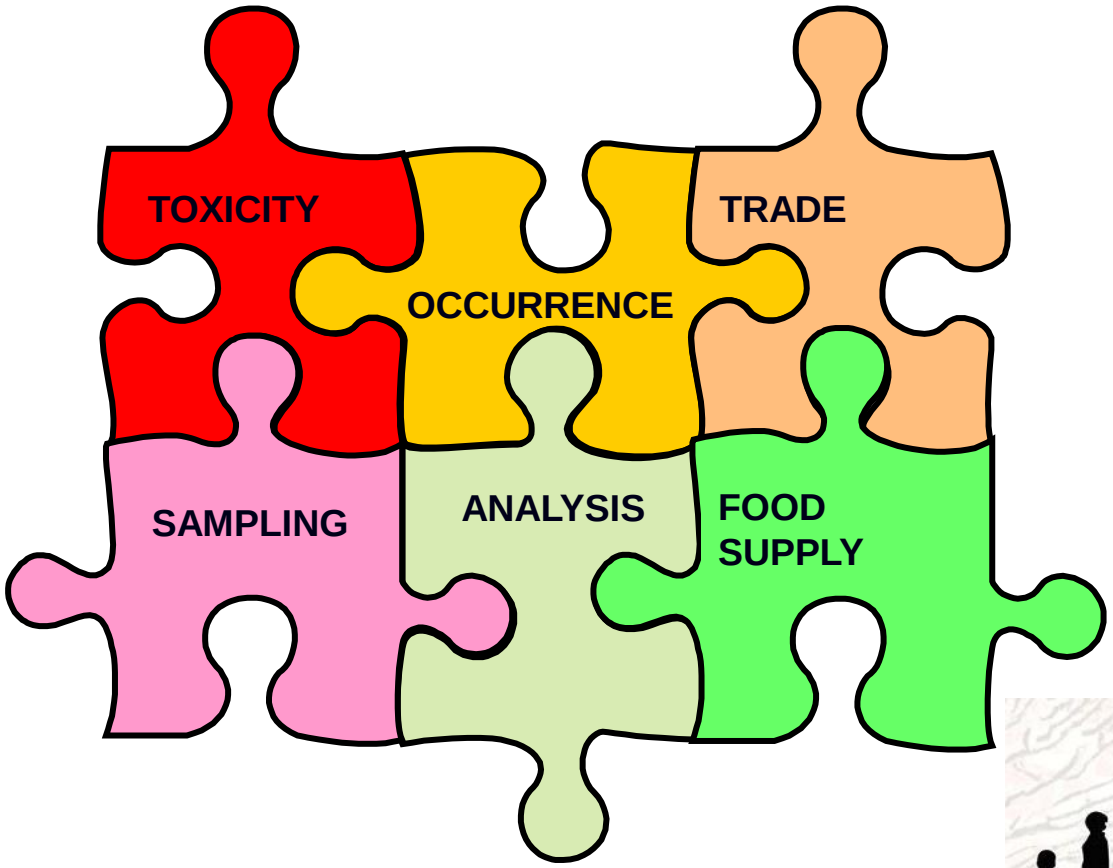
Patulin

HT2 and T2 in oats
Ochratoxin A in dried fruit and cereals
Aflatoxins in nuts

Fumonisins

Regulatory puzzle

Many factors play a role in the decision-making process required for setting limits.

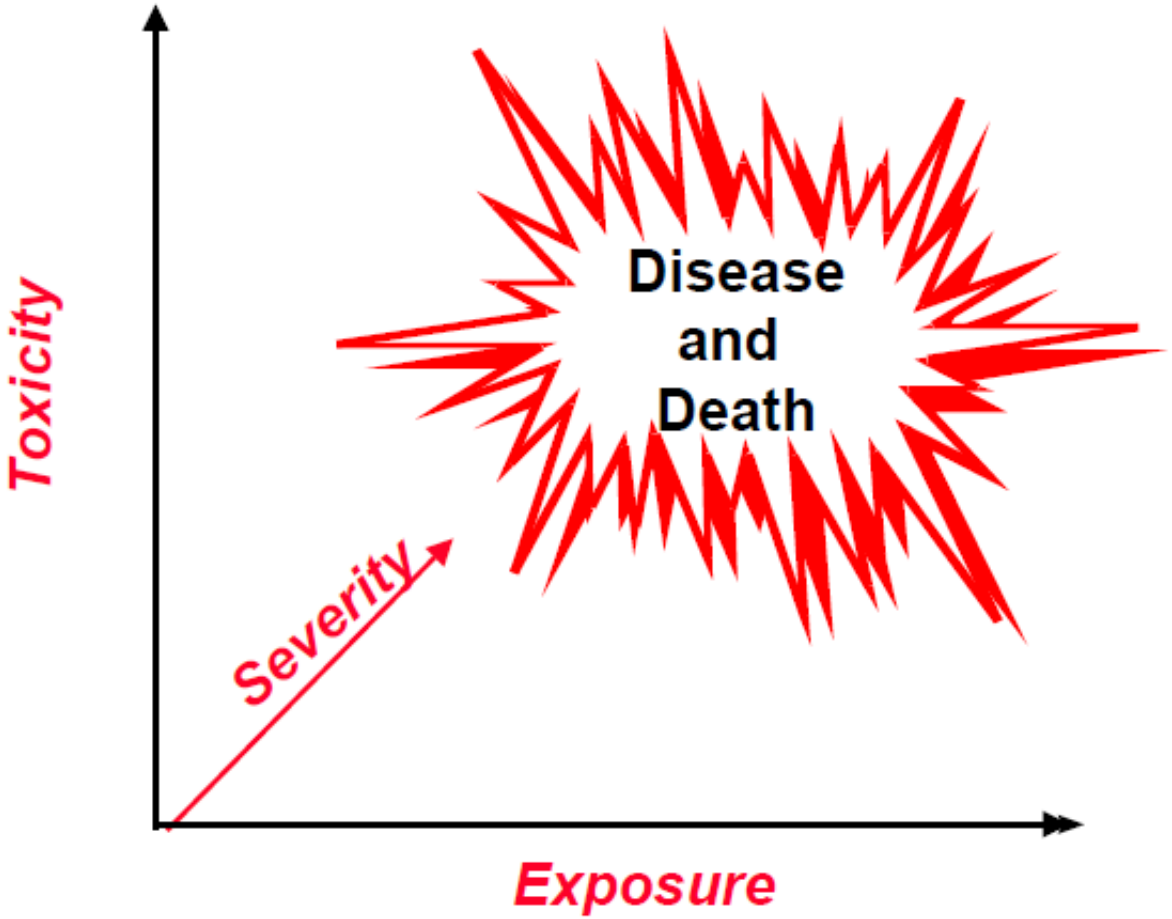


Toxicological Risk assessment
identification,
metabolic pathway,
acute or chronic effects,
occurrence,
uptake and susceptibility of consumers,
multiple commodities,
global dietary patterns

Safety Measurements

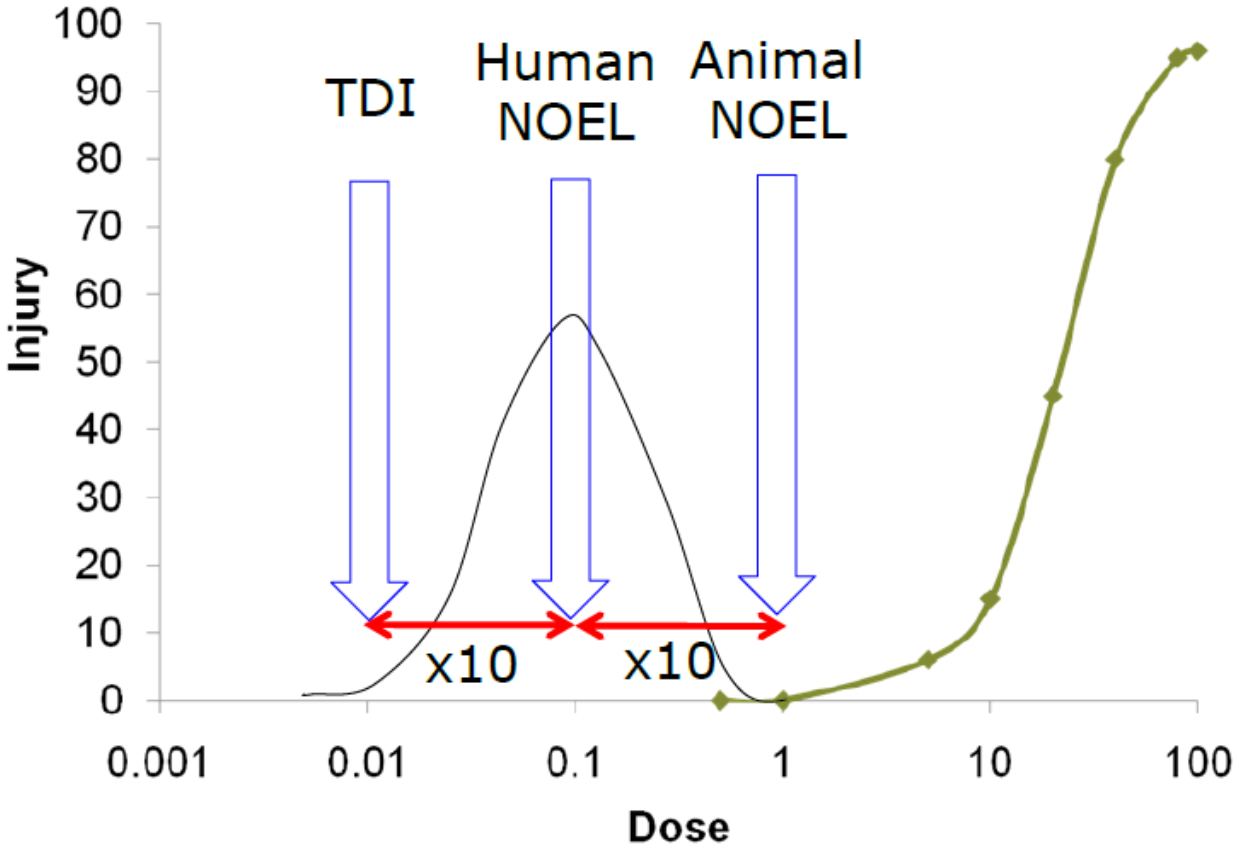
- Safe limits are reported as TDI (Tolerable Daily Intake)
- In theory where a TDI is established this level of contaminant is safe to consume every day for life
- TDIs are based on NOEL (No Observable Effect Limit) from animal studies using a range of contaminant doses
- Divide by 10 as different species
- Divide by 10 for range of sensitivity within a species
- Based on body weight, reported as µg / kg body weight / day
- For genotoxic carcinogens no level is deemed safe – use ALARA principle (as low as reasonably achievable)

Chemical Hazards in Food



Paracelsus
(1493-1541)
Dosis facit venenum
"The dose makes the poison"

Tolerable Daily Intake calculation



Exposure Measurements

- Risk = Toxicity x Exposure
- Exposure very difficult to calculate
- Determine levels in different foodstuffs (usually very wide range with highly skewed distributions)
- Determine dietary intake (highly variable)
    - Diverse international cuisine
    - Dietary restrictions eg glucan intolerance
    - “Extreme” consumers (95th%)

- Infants often most at risk as consume relatively large amounts of food for their low bodyweight

- Future method – Biomarkers eg DON in urine – can monitor exposure in population as a whole and in discrete sub-populations

Food safety zero tolerance limits

- In Food safety policy, zero tolerance means that if any harmful substance is found on a food product, be it chemical, microbiological, or other, then the product will be considered unfit for human consumption.

- Zero tolerance limits are important in order to protect not only human health but environmental health as well.

- The USDA sets a zero tolerance limit for visible signs of faecal contamination on meat and poultry.

Regulations on food additives

- Food additives are chemicals that are added to food to enhance appearance, flavour and shelf-life.
- The potential health risks of food additives has caused much controversy. Eating a high amount of an additive may be harmful, but at a lower level it may be perfectly safe.
- Additives are controlled by law, and can only be used following stringent tests and approval by an independent committee of scientists and medical experts.
- The tests will determine the level, expressed in mg per kg of body weight per day (mg/kg bw/day), that an additive can be used without having a harmful affect on human health.
- Food additives are always included in the ingredients lists of foods in which they are used. Product labels must identify the function of the additive used and the specific substance used, either by name or number.

Regulatory limits for pathogens in food

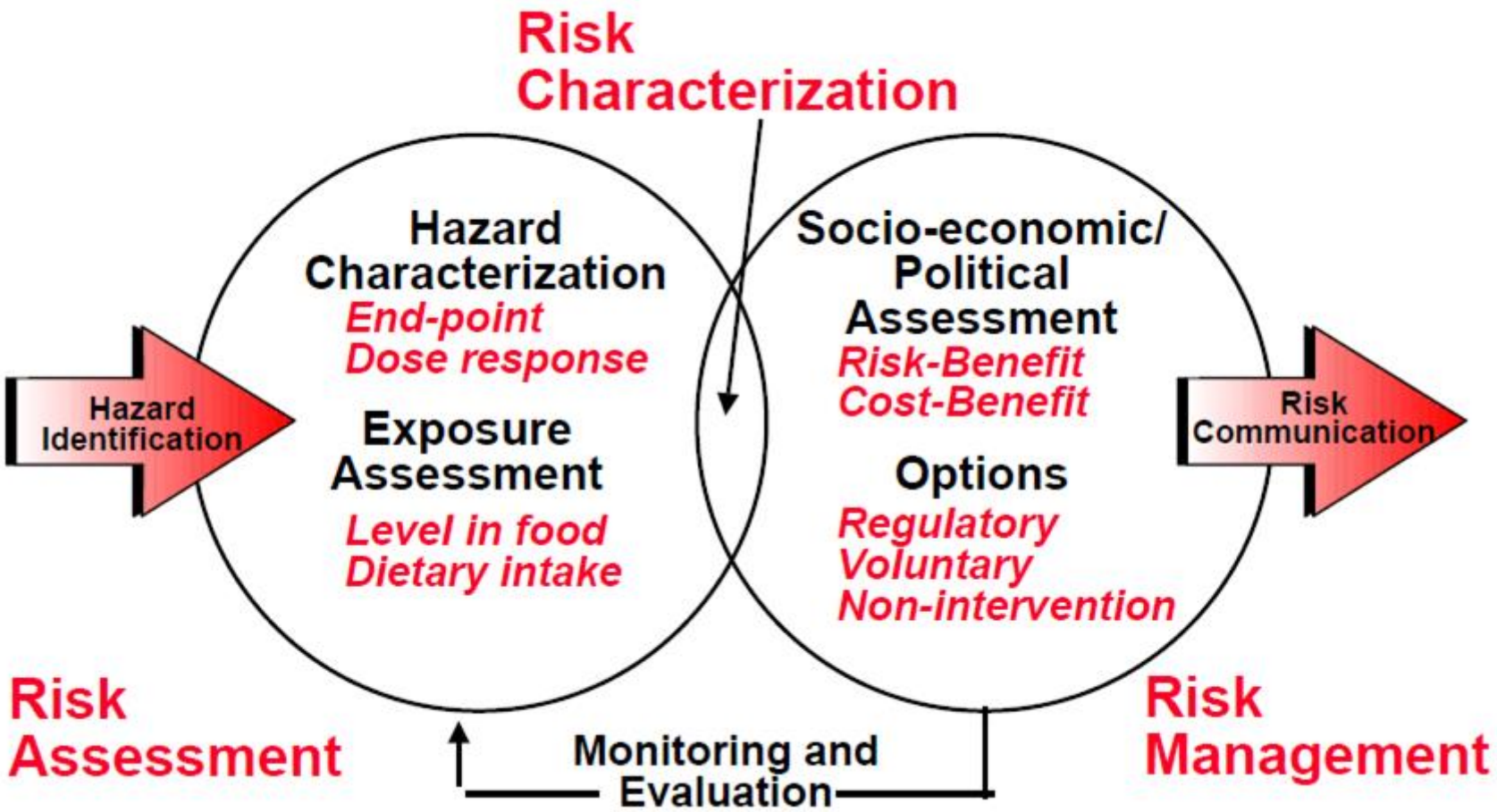
- Foodstuffs should not contain micro-organisms or their toxins or metabolites in quantities that present an unacceptable risk for human health.

- Microbiological limits are set for pathogens in foodstuffs. These are the maximum permissible levels of foodborne microorganisms that pose a risk to human health in nominated foods, or classes of foods. These limits differ for various types of pathogens and food products.

- Microbiological quality is related to the aerobic colony count, number of indicator organisms and the presence/ number of pathogens determined.

- Microbiological quality is categorised as satisfactory, acceptable, unsatisfactory and unacceptable/potentially hazardous.

Summary: Risk Analysis



Sampling and Analysis

- Pre –harvest

- Post Harvest Storage

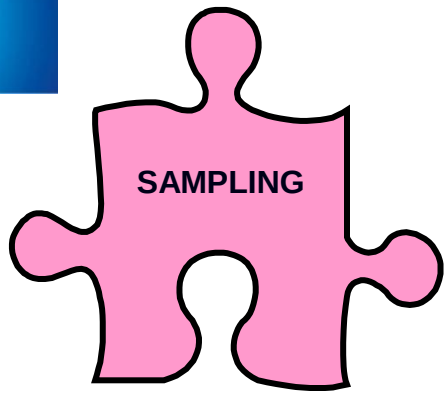
- Animal Feed

- Food Products

Heterogeneous Occurrence

Devised Sampling Plan

Higher frequent sampling

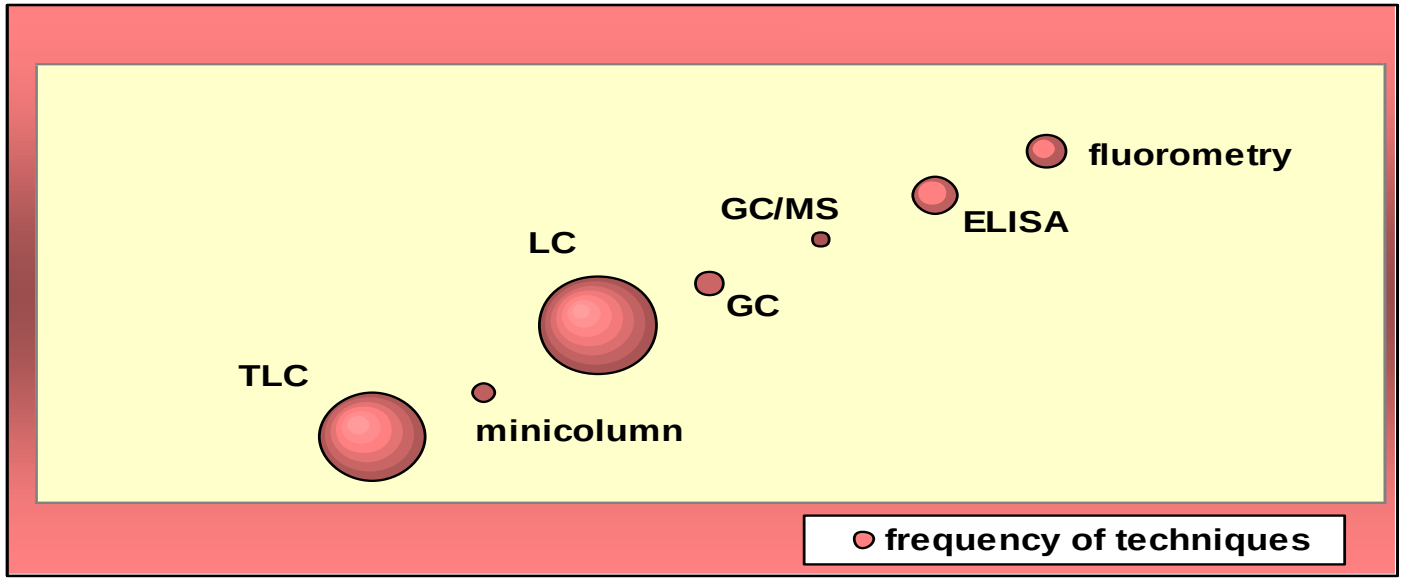


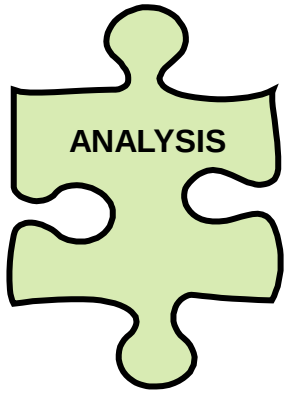
Measurement of Contaminants

Bioanalytical and Analytical methods are required to:

Determine concentrations of the contaminants in foods to evaluate safety and to enforce legislative requirements

Many different techniques are used in contaminant analysis.





However, it is vital to ensure that laboratories use methods with comparable levels of performance for harmonisation of standards

References

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