Risk Assessment of Chemicals in Foods- WHO Principles and Methods

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OUTLINE

- Principles of Risk Analysis
- Hazard Identification and Characterization
- Exposure Assessment
- Risk Characterization(ADI)
- Additional Risk Assessment Tools.

Scientific Advice to Member States of FAO and WHO

- IPCS/WHO TOOLS OF RISK ASSESSMENTS
- JECFA- The Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives ()
- JMPR-Joint FAO/WHO Meeting on Pesticide Residues (JMPR) have provided scientific advice to Member States of FAO and WHO
- Codex

K ASSESSMENT PRINCIPLES

Ensure food available commercially are safe for the consur
and do not pose unnecessary **risk**.

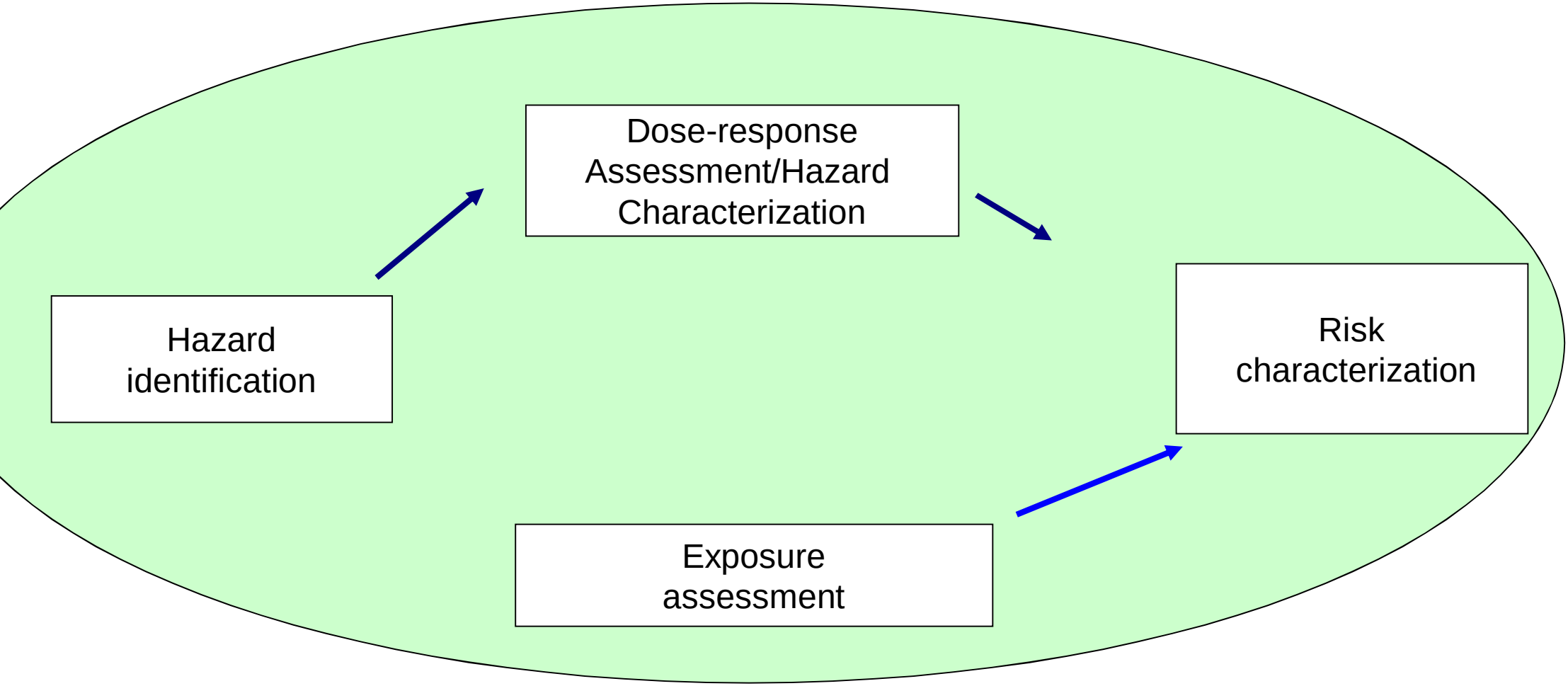
What is risk?

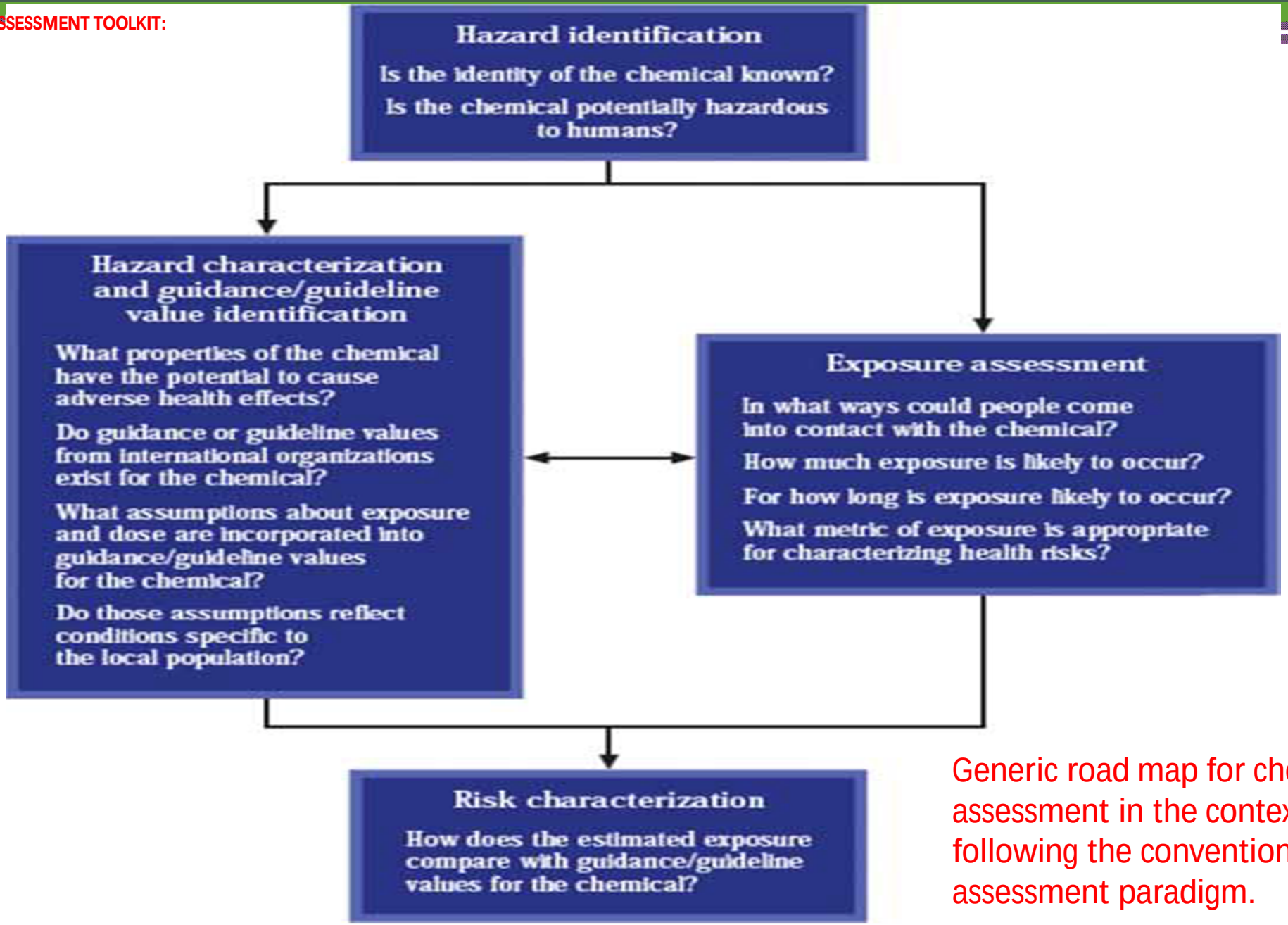
RISK ≠ HAZARD

- Risk is defined as likely hood of harm in defined circumstances.
- Hazard –Potential to cause harm.

RISK = EXPOSURE X HAZARD

Risk Assessment- A scientifically based process





Generic road map for chemical risk assessment in the context of the T following the conventional risk assessment paradigm.

Step 1 - Hazard Identification

What is known about the chemical already

- Information from the supplier
- Regulatory approvals
- Literature search on the chemical
    1. Standard Toxicology Studies
    2. Investigative/research publication
    3. Media stories
- Use of chemical other than food
- Anecdotal information

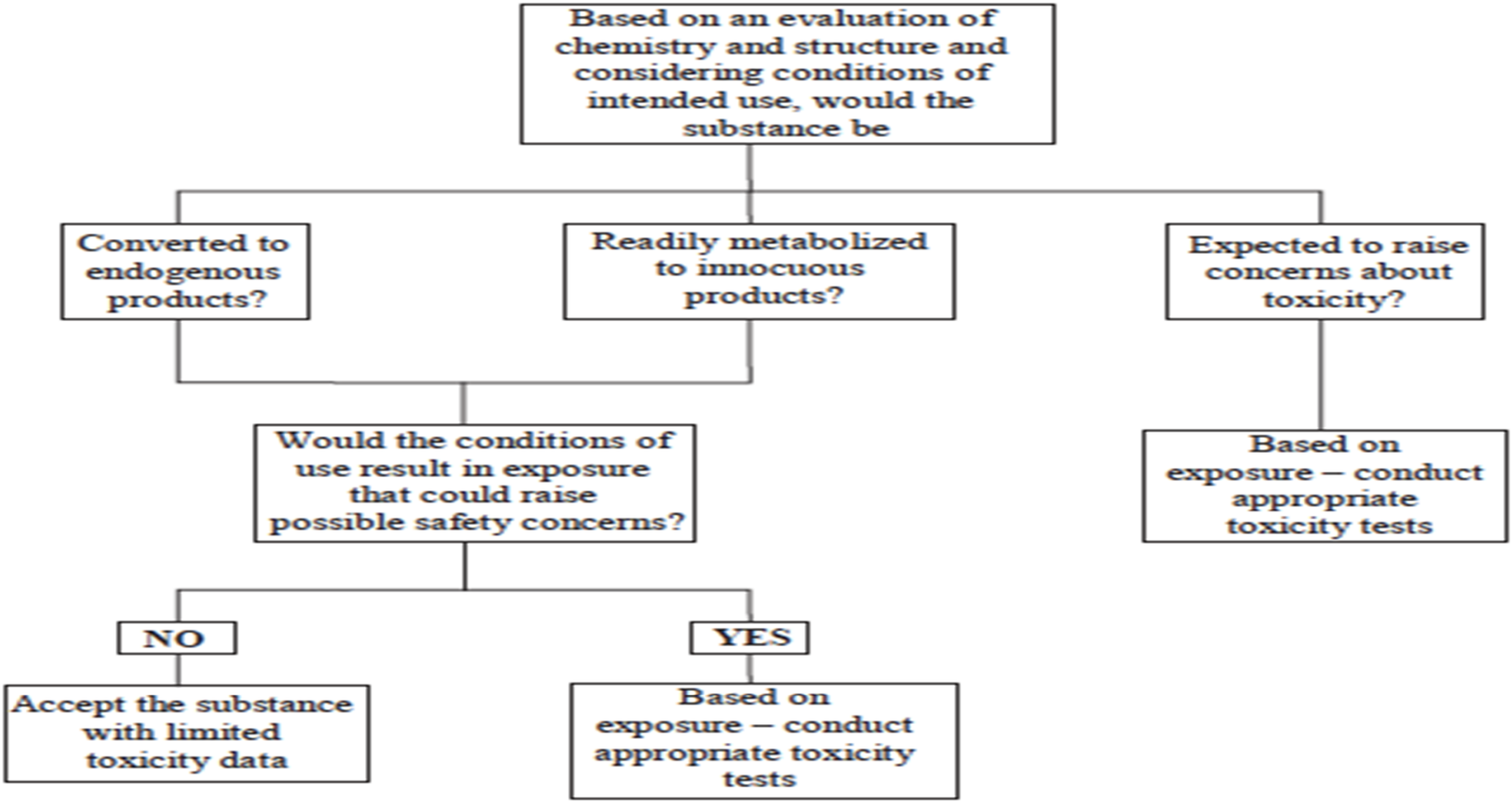


Fig. 4.1. A stepwise approach to assessing toxicity testing needs

Step 1 - Hazard Identification

Build a picture to determine what the safety ssues are

and

what package of safety support might be needed.

Step 1 - Hazard Identification

1. For most ingredients –Toxicological data already exists
2. For some ingredient expert toxicological evaluation are published- EFSA, FDA, JECFA.JMPR,,RIFM,FEMA,GRAS
3. Where ever possible, existing data are used in safety assessment
4. All available data are(manufacturer, expert bodies, publications) evaluated and their robustness are established.
5. QSAR evaluation, including **read across** to similar chemicals, may be used for initial evaluation.
6. Other considerations such as history of safe use or Human Clinical data can be used in a weight of evidence approach.

Step 1 - Hazard Identification

- If data does not exist or inadequate, toxicological testing may be conducted to identify and characterise the toxicological hazard.
- Alternative to Animal Testing- as far as possible.
- Should be conducted as per OECD and GLP

Step 1 - Hazard Identification

Animal Studies

- Mouse
- Rat
- Rabbit
- Guineapigs

Step 1 - Hazard Identification

DATA ON TOXICITY

- Acute Oral
- Acute Dermal
- Acute Inhalation
- Primary Skin Irritation
- Irritation to Mucous Membrane
- Sub Chronic studies through Oral,Dermal and inhalation route-90 days

Step 1 - Hazard Identification

DATA ON TOXICITY

- Chronic Toxicity/Carcinogenicity(Two years in Rat/18 months mice)
- Effect on reproduction
- Developmental Toxicity
- Neurotoxicity
- Genotoxicity Studies
- ADME in Animals (Pharmacodynamics and toxicokinetics)
- Information on Effect on Human being

Step Two
Dose-Response Assessment

Toxicity Determination

- Review all studies
- Identify critical study - adverse effect at the lowest dose
- Identify the No Observed Effect Level **NOEL** or No Observed Adverse Effect Level **NOAEL**,
- Lowest Observed Adverse Effect Level **(LOAEL)**

The Dose Makes the Poison

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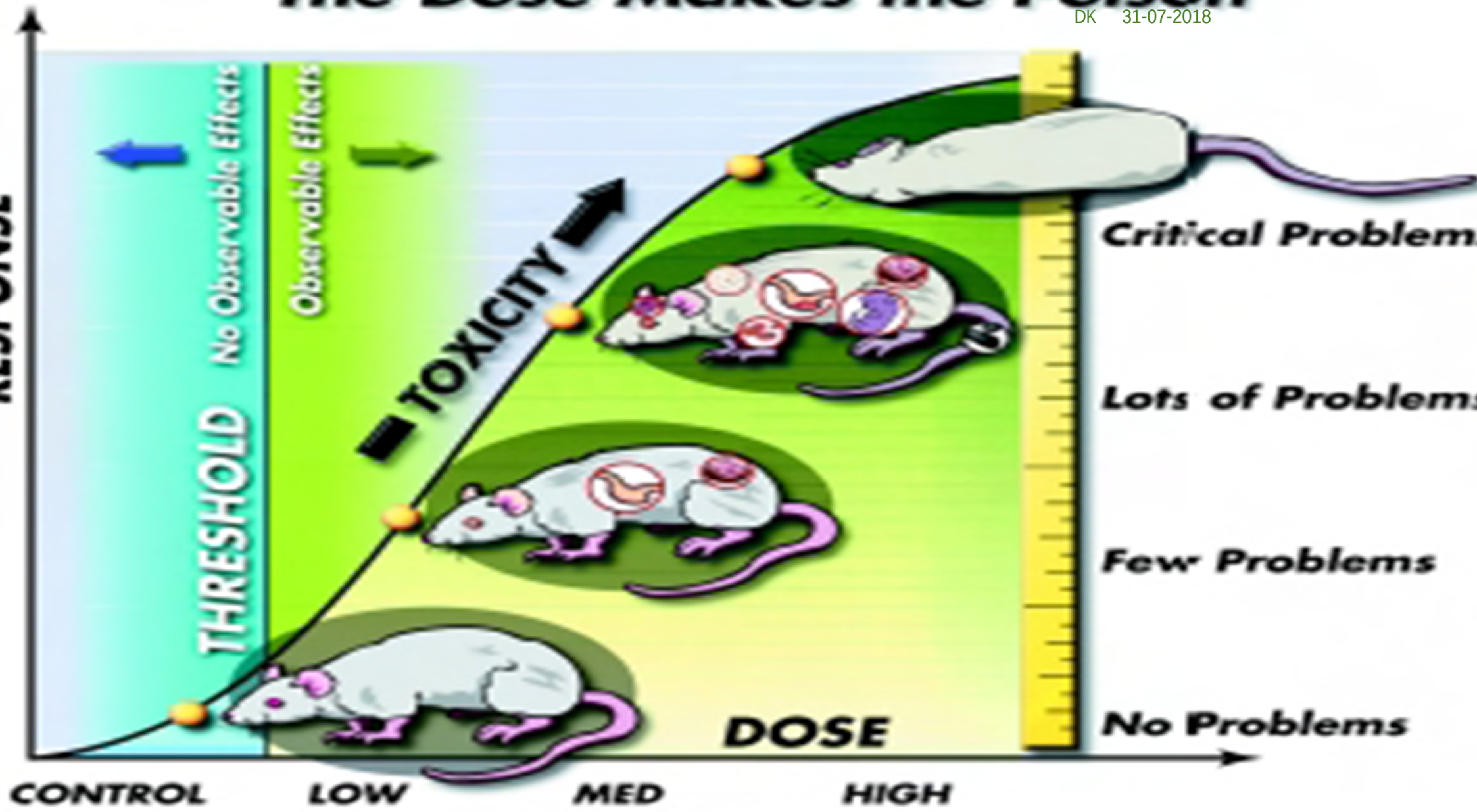

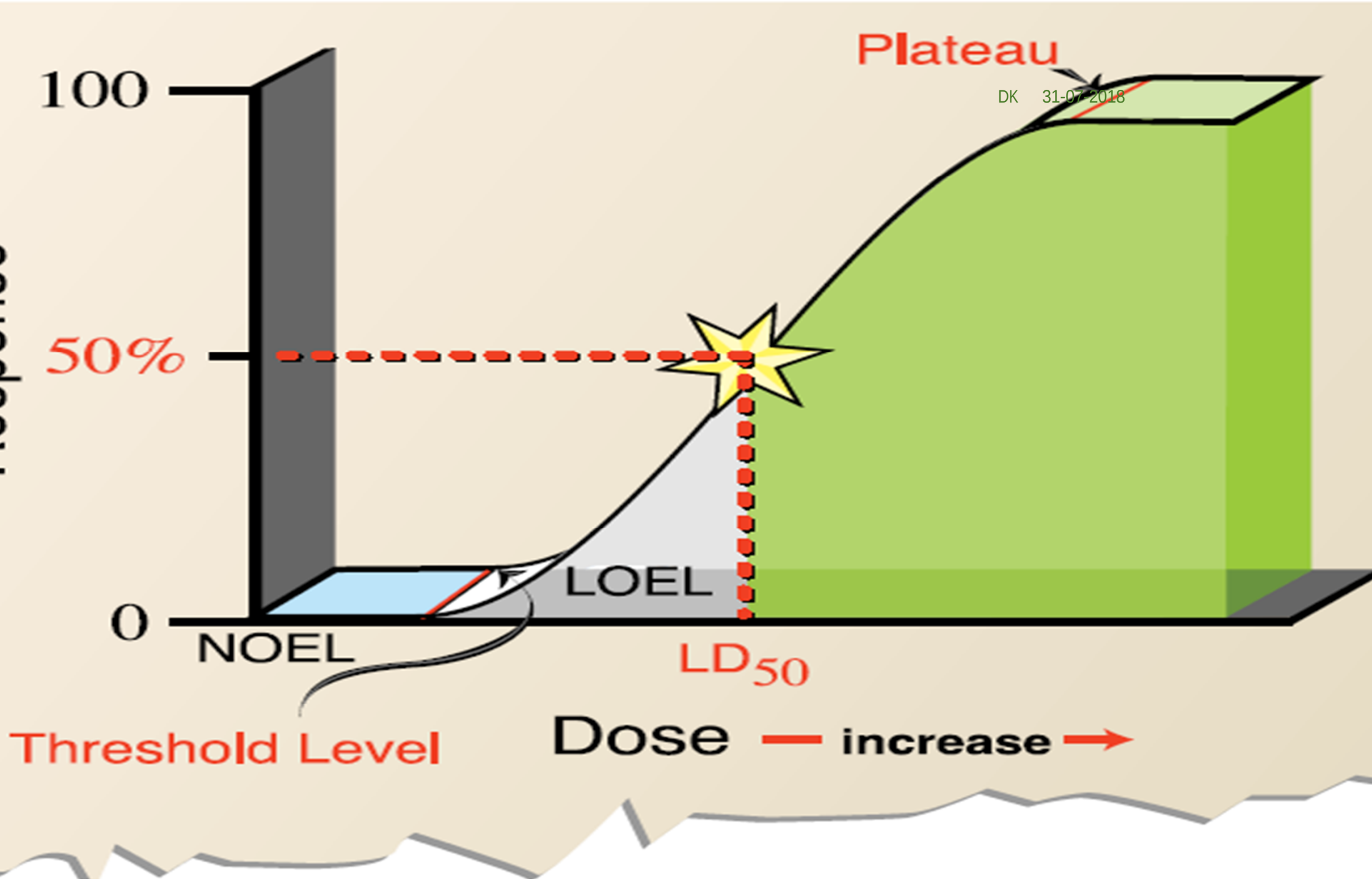
Plateau
100
50%
0
LOEL
NOEL
LD_{50}
Threshold Level
Dose — increase →

Dose-response Assessment and Endpoint Selection

- **Endpoint:** Toxic Effect upon which the risk assessment is based

- **Lowest Observed Adverse Effect Level (LOAEL):** Lowest dose from a study at which adverse toxic effects were observed

- **No Observed Adverse Effects Level (NOAEL):** The Highest data point/ dose below the LOAEL at which no adverse toxic effects are observed.

Determining Safe Levels

- The NOAEL is considered the " safe level " for that chemical in the species studied
- The animal NOAEL is **not necessarily the " safe level " for humans, because:**
  - humans may be more/less sensitive to the substance than the animals studies
  - Humans have more genetic, health, age and variabilities, which may affect individual human reactions

Hence extrapolation from animals to human being is required

Safety Factors

- Effects vary between animals of different species
- Effect vary from person to person.
- To account for this variability, uncertainty factors are built into the risk assessment.
- These uncertainty factors create an additional margin of safety for protecting people who may be exposed to the pesticides.

The use of uncertainty or safety factors

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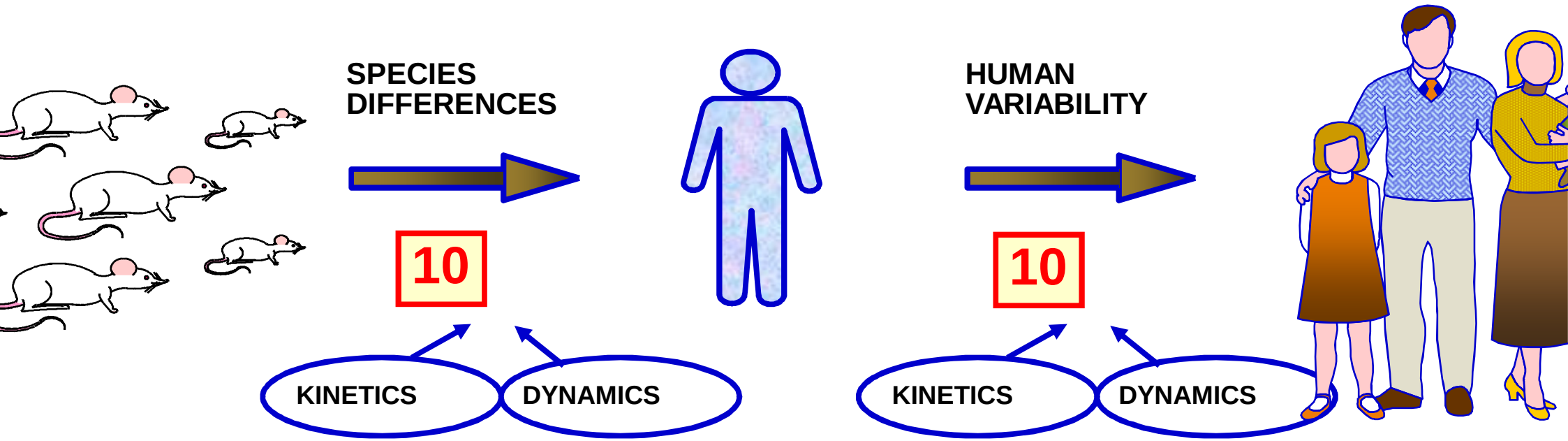

Uncertainty or safety factors are used to extrapolate from a group of test animals to an average human and from average humans to potentially sensitive sub-populations. Up to an additional 10x to protect children

ncertainty and Safety Factors DK 31-07-2018

- Generally 100 X unless:
  - A smaller factor can be shown to be protective, or
  - A larger factor is clearly needed
- Maximum = 3000
- Chemical Specific Adjustment Factor(CSAF)

Step Four- Risk Characterization

Dietary Intake and the Risk Assessment

- Detailed daily consumption of food
- Different types of consumer
  (infants, adult, elderly, vegetarians).
- Sources –National Survey,GEMS

Dietary Exposure: Calculation

$$\text{Exposure} = \frac{\text{Residue} \times \text{Consumption}}{\text{Body weight}}$$

$$\frac{\text{mg chemical}}{\text{g bw-day}} = \frac{\text{mg chemical}}{\text{Kg food}} \times \frac{\text{grams food}}{\text{day}} \times \frac{\text{Kg food}}{\text{1000 g food}} \times \frac{1}{\text{Kg BW}}$$

Correction factor

ACCEPTABLE DAILY INTAKE-(ADI)

- Should protect against the chronic effects of an upper percentile of the time-weighted averaged daily intake per person
- It is assumed that the chronic effects depend largely on this measure; are not significantly influenced by short-time fluctuations

ADI= NOAEL÷ 100

EXPOSURE < ADI

EXPOSURE > ADI

ADDITIONAL RISK ASSESSMENT TOOLS

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1.History of Safe Use (Applied to safety assessment of Novel Foods)

Characterisation

- Biology(Genetic Diversity,Origin)
- Geographic distribution
- Composition

Details of Use

- Preparation and Processing
- Purpose/Indication
- Pattern of consumption
- Intake(Range,Population)
- Known limitations of use(Cultural practices)

Previous Human Exposure

- Population Diversity
- Genetic back ground
- Age Group

Health Effects

- Evidence from human exposure
- Known adverse effect
- Case report

Potential Hazards

- Tox data
- Nutrition data, Allergen

ADDITIONAL RISK ASSESSMENT TOOLS

2.THRESOLD FOR TOXICOLOGICAL CONCENTRATION (TTC)

(Thresold of exposure for chemicals of known structure below which there is no appreciable risk to human being)

ATEGORY		Description	TTC (mg/person/day
er I	Low Toxicity	Substances with simple structure for which efficient mode of detoxification exist in our body	1.8
er II	Modera te Toxicity	Substances less innocuous than in class I , but do not contain structural features suggestive of toxicity like in class III	0.54
er III	High Toxicity	Substances suggesting significant toxicity or containing reactive functional grp.	0.09

Useful Approach for Risk Assessment –Food Chemicals WHEN

- Present in food at low concentration
- Little or no toxicity data

EXCLUSION

- **High potency carcinogens**
- **Neurotoxicants**
- **Allergens**
- **EDS**

Munro et al (1996, 1999), Kroes et al (2000, 2004)).

ILSI Europe Concise Monograph Series (2005). Threshold of toxicological concern

Q & A

No Conflict of Interest

Thank you very much!

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