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
Ensure food available commercially are safe for the consumer and do not pose unnecessary risk.
What is risk?
RISK ≠ HAZARD

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

RISK = EXPOSURE X HAZARD
Risk Assessment- A scientifically based process

- Hazard identification
- Exposure assessment
- Dose-response Assessment/Hazard Characterization
- Risk characterization
Generic road map for chemical risk assessment in the context of the Toolkit 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
Based on an evaluation of chemistry and structure and considering conditions of intended use, would the substance be

- Converted to endogenous products?
- Readily metabolized to innocuous products?
- Expected to raise concerns about toxicity?

Would the conditions of use result in exposure that could raise possible safety concerns?

- NO
  - Accept the substance with limited toxicity data
- YES
  - Based on exposure – conduct appropriate toxicity tests

Fig. 4.1. A stepwise approach to assessing toxicity testing needs
Step 1 - Hazard Identification

Build a picture to determine what the safety issues 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 ingredients expert toxicological evaluation are published - EFSA, FDA, JECFA, JMPR, RIFM, FEMA, GRAS
3. Wherever possible, existing data are used in safety assessment
4. All available data (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

TOXICITY

THRESHOLD

DOSE

CONTROL  LOW  MED  HIGH

No Observable Effects  Observable Effects

No Problems  Few Problems  Lots of Problems  Critical Problems
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 studied.
  - 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
- Effects 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.
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.
Uncertainty and Safety Factors

- 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: Calculations

Exposure = Residue × Consumption

\[
\text{mg chemical} \times \frac{\text{Kg food}}{\text{Kg BW}}
\times \frac{\text{grams food}}{\text{day}}
\times \frac{\text{Kg food}}{1000 \text{ g food}}
\times \frac{1}{\text{Kg BW}}
\]

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

\[ \text{ADI} = \frac{\text{NOAEL}}{100} \]

\[ \text{EXPOSURE} < \text{ADI} \]

\[ \text{EXPOSURE} > \text{ADI} \]
ADDITIONAL RISK ASSESSMENT TOOLS

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 background
- 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. THRESHOLD FOR TOXICOLOGICAL CONCENTRATION (TTC)
(Threshold of exposure for chemicals of known structure below which there is no appreciable risk to human being)

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>Description</th>
<th>TTC (mg/person/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cramer I</strong></td>
<td>Low Toxicity Substances with simple structure for which efficient mode of detoxification exist in our body</td>
<td>1.8</td>
</tr>
<tr>
<td><strong>Cramer II</strong></td>
<td>Moderate Toxicity Substances less innocuous than in class I, but do not contain structural features suggestive of toxicity like in class III</td>
<td>0.54</td>
</tr>
<tr>
<td><strong>Cramer III</strong></td>
<td>High Toxicity Substances suggesting significant toxicity or containing reactive functional grp.</td>
<td>0.09</td>
</tr>
</tbody>
</table>

**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

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

No Conflict of Interest

Thank you very much!

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