Current Issues for Nutrition Safety in Asia: Setting Tolerable Upper Intake Levels: Approaches and Challenges

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Outline of presentation

- Nutrition safety
- Risk Analysis Frame Work
- Nutritional Risk Assessment – **Approaches**
- A Model for Establishing Upper Levels of Intake for Nutrients and Related Substances
- Significant difference between nutrient and non-nutrient risk
- **Challenges**
Health and Nutrition Consciousness

- Populations around the world are having Health Problems, both under and over nutrition.

- Nutrition is one of the main factors that has a significant impact on health.

- People tend to take more nutrients from products according to extensive commercial promotion, if no proper regulation.
Large number of products are in the market, especially food supplement products, with almost unlimited level of nutrients.

Vitamin and mineral food supplements are the main products in the market with often used mega dose.

Therefore, it is essential to find ways and means to regulate the maximum level of nutrient intake.

Risk assessment is the main principle used to set the tolerable maximum intake for safety.
Risk Analysis Framework

Risk Assessment
- Science based

Risk Management
- Policy based

Risk Communication
- Interactive exchange of information and opinions concerning risks
Components of non-nutrient conventional Risk Analysis

Risk Assessment
- Hazard Identification
- Hazard Characterization
- Exposure Assessment
- Risk Characterization

Risk Management
- Risk Evaluation
- Option Assessment
- Option Implementation
- Monitoring & Review

Risk Communication
Science based
Interactive and ongoing exchange of information and opinions

Policy based
Nutritional Risk Assessment - Approaches

- Codex *procedural manual* specified the principle of risk analysis to be used in the work of CCNFSDU

- FAO/WHO published in 2006: **A Model for Establishing Upper Levels of Intake for Nutrients and Related Substances**
  
  - Form the basis for setting the tolerable maximum level of nutrient intakes
  
  - Conventional risk assessment of chemicals is useful for Nutrient risk assessment but needed modification
Nutrient-related homeostatic mechanisms are related to the unique dual risks that are posed by inadequate intake of an essential nutrient substance in one case and by excessive intake of the substance in the other case.

In contrast, the relationship for risk associated with non-nutrients (e.g. food additives, contaminants, and pesticides) is notably different.

The risk for non-nutrient substances reflects only an increase in risk with an increase in intake, i.e. it is characterized by one curve.
Note: Modified from Environmental Health Criteria 228 (IPCS, 2002).
### Examples of Homeostatic Mechanisms for Nutrient Substances

<table>
<thead>
<tr>
<th>Nutrient substance</th>
<th>Homeostatic mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>Absorption increases or decreases with changes in iron stores</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Renal conversion of the nutrient substance to the active hormone is regulated by the blood calcium level</td>
</tr>
<tr>
<td>Calcium</td>
<td>Intestinal absorption, deposition and release from bone, and urinary excretion of calcium are under complex physiologic control, in which active vitamin D hormone plays a key role</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Renal excretion of the vitamin occurs when the blood level exceeds a threshold value</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>Storage of excess vitamin A increases in the liver until the storage capacity is exceeded</td>
</tr>
</tbody>
</table>
Safe Range of Intake

Risk of inadequacy

RDA

UL

NOAEL

LOAEL

0

0.5

1.0

Safe Range of Intake

Observed Level of Intake

10/01/56

Definitions for four key terms:

- An **adverse health effect** is a *change in morphology, physiology, growth, development, reproduction or life span* of an organism, system, or (sub)population that results in an impairment of functional capacity.

- **Hazard** is the *inherent property of a nutrient or related substance to cause adverse health effects* depending upon the level of intake.
Habitual intake is the long-term average daily intake of the nutrient substance.

The upper level of intake (UL) is the maximum level of habitual intake from all sources of a nutrient or related substance judged to be unlikely to lead to adverse health effects in human.
Non-nutrient Risk Assessment
- Hazard Identification
- Hazard Characterization
- Exposure Assessment
- Risk Characterization

Nutrient Risk Assessment
- Hazard identification + Hazard characterization
- Dietary intake assessment
- Risk characterization
**FAO/WHO Model**

**Key Topic Areas**

- Problem formulation
- Hazard identification
- Hazard characterization

**Key Activities**

- Foster interactions between risk managers and risk assessors to ensure common understanding of the problem and to refine problem formulation as needed.

- Define data search strategy a priori.
- Identify adverse health effects and related levels of intake.
- Evaluate and summarize data objectively.
- Determine basis for selection of the critical adverse health effect.
- Clarify intake–response relationship to identify benchmark intake (BI), no observed adverse effect level (NOAEL), or lowest observed adverse effect level (LOAEL).
- Adjust the BI, NOAEL, or LOAEL for uncertainty, and establish upper level of intake (UL).
- As necessary, adjust UL derived for a studied subpopulation to derive ULs for unstudied age-sex/lifestyle subpopulations.

- Specify need for total dietary intake or targeted dietary intake data.
- Specify need for habitual intake or acute intake data.
- Modify or add to available composition data as needed.
- Take into account strengths and limitations of available consumption data.
- Determine method to estimate intake of nutrient substance.
- Make statistical adjustments to estimated intakes as appropriate.
- Provide caveats for estimates based on uncertainties, and describe the impact of uncertainties.

- Integrate hazard characterization and dietary intake assessment.
- Identify types of information needed by managers and the presentation format.
- Include relevant descriptions of the nature of the critical adverse health effect and other effects as appropriate, severity and reversibility of effects, and nature of threshold levels and dose–response relationship.
- Describe the impact of uncertainty on conclusions.
Nutrient hazard identification/characterization

- The data evaluation relevant to hazard identification and characterization is iterative: it requires dialogue and refinement activities among the assessment participants. The process begins with the identification of adverse health effects associated with the nutrient substance and makes use of human, animal, and in-vitro data.
• A pivotal point in the assessment process is the selection of the critical adverse health effect.
• This is the effects upon which a set of ULs for the various age/sex/life stage (sub)populations is based.
• This usually is the adverse health effect that occurs at the lowest level of intake within the (sub)population of interest—or at the lowest experimental dose if only animal data are available.
Identifying Adverse Health Effects: Sequence of ‘effects’ in increasing order of severity

1. Biochemical changes within the homeostatic range and without indication of adverse sequelae?

2. Biochemical changes outside the homeostatic range without known sequelae?

3. Biochemical changes outside the homeostatic range that represent a biomarker of potential adverse effects due to excess?

4. Clinical features indicative of a minor but reversible change?

5. Clinical features of significant but reversible effects?

6. Clinical features indicative of significant but reversible organ damage?

7. Clinical features indicative of irreversible organ damage.
Derivation of the UL then moves to assessing the intake–response relationship for the critical adverse health effect.

The nutrient risk assessor determines a no observed adverse effect level (NOAEL) or, alternatively, a lowest observed adverse effect level (LOAEL).

Following this, the important step of accounting for uncertainties must occur; this step requires careful and detailed scientific judgement on the part of the nutrient risk assessor.
Safe Range of Intake

UL = NOAEL / UF₁ or LOAEL / UF₂   UF₂ > UF₁
Evaluate data for evidence of no toxicity at that intake

**Toxicity**

- Dose-response assessment to identify NOAEL or LOAEL
- Select an uncertainty factor (UF) for data quality
- Calculate $\text{UL} = \frac{\text{NOAEL (or LOAEL)}}{\text{UF}}$

**No toxicity**

- If no evidence of toxicity, a NOAEL or LOAEL cannot be set and no UL can be calculated
- **Apply Highest Observed Intake Method (HOI) = the highest level with adequate evidence of no toxic effects – use HOI instead of UL**
Established toxicity: Classic UL method applied

No established toxicity: OSL (HOI) method applied
Dietary Intake Assessment

- If available, intake data obtained from individuals are the most useful type of data for dietary intake assessment because they allow the estimation of an intake distribution. However, that such data are rare in most regions of the world.

- Special considerations were given to strategies for combining data from different sources in order to estimate intakes.
Nutrient risk characterization

Risk characterization is final stage of nutrient risk assessment, the outcomes of hazard characterization are combined with the dietary intake assessment in order to describe the overall nature of the risk and its magnitude.

It should be designed to meet the needs of risk managers and facilitate their decision-making processes.

Reviewing the problem formulation, can be very useful in determining how nutrient risk characterization can meet the risk manager’s specific needs.
Global relevance

*Scientific/medical data*
- Biological and physiological information

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Population relevance

*Population-derived data*
- Intake estimates, population conditions

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Hazard identification

Hazard characterization/UL

Exposure assessment

Risk characterization
- **Challenges:**

  - To accumulate **adverse effect data of nutrients** with reliable and acceptable scientific studies, from animals, non-animal, epidemiological and human observations.

  - How to obtain **intake data from individuals** which are the most useful type of data for dietary intake assessment.

  - The **harmonization** of Tolerable UL of intake among countries, regions or worldwide.
- Harmonization of technique and methodology for the study of nutrient intake from regional and national food consumption survey of well-designed studies intended to determine the risk of nutrient substance intake.

- Capacity building of the competent risk scientists to perform the nutrient risk assessment

- Communicating among risk assessors, risk managers (regulators) and all the stakeholders, particularly consumers.
**Suggested reading for further detail:**


2. WORKSHEETS USED BY ACCSQ TRADITIONAL MEDICINES AND HEALTH SUPPLEMENTS SCIENTIFIC COMMITTEE (ATSC) FOR THE ESTABLISHMENT OF THE ASEAN MAXIMUM LEVEL OF VITAMINS & MINERALS IN HEALTH SUPPLEMENTS
   For the period between 6th – 15th ATSC Meeting
   (29th November 2009 – 25th June 2012)


5. PRINCIPLES FOR THE ASSESSMENT OF RISKS TO HUMAN HEALTH FROM EXPOSURE TO CHEMICALS, EHC 210
Other national region documents

6. EFSA-SCF: European Food Safety Authority, European Union and (the former) Scientific Committee on Food, European Commission;

7. EVM: Expert Group on Vitamins and Minerals, Food Standards Agency, United Kingdom;

8. IOM: Institute of Medicine of the National Academies, United States of America and Canada.
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สวัสดีครับ / Thank You