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Expert Consultation On Nutrient Risk Assessment For Determination Of Safe Upper Levels For Nutrients New Delhi, India, 4 December 2015

Nutrient Risk Assessment & Upper Levels in the EU

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Vitamins and minerals in foods in the EU

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- 1991-1999. Adoption of Directives on Foods for infants and young children, Foods for Special Medical Purposes, Foods for weight reduction
- 2002. Adoption of Directive on Food Supplements
- 2006. Adoption of Regulation on Addition of Vitamins and Minerals and of certain Other Substances

Vitamins and minerals in foods in the EU

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Aim of the specific rules ➔ safety of products

- Ensure adequate composition of products (minimum amounts for micronutrients)
- Ensure that consumption of products did not pose a risk to health (maximum amounts for micronutrients)

Risk Analysis

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Consists of:

- Risk Assessment-by risk assessor (scientific advisory body)
- Risk Management-by risk manager (regulators)
- Risk Communication-coordinated between risk assessor and risk manager

European Commission Mandate to Risk Assessor

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To Scientific Committee for Food (SCF) and European Food Safety Authority (EFSA)

1) to review the upper levels of daily intakes of individual vitamins and minerals that are unlikely to pose a risk of adverse health effects; and

2) to provide the basis for the establishment of safety factors, where necessary, for individual vitamins and minerals which would ensure the safety of fortified foods and food supplements containing these nutrients.

Risk Analysis for Nutrients

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- Nutrient risk analysis addresses nutrient and related substances and the risk to health from their inadequate and/or excessive intake.
- Nutrient risk analysis applies the same general approach as traditional food safety risk analysis to consideration of excessive intakes of nutrients and related substances.

Codex Nutritional Risk Assessment Guidelines, 2010

Risk Assessment for nutrients

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"Vitamins and (essential) minerals are micronutrients which are essential components of the human diet and the human body. Like other chemical substances, micronutrients may have adverse effects if consumed in excessive amounts. However, when evaluating the adverse effects of micronutrients it is necessary to take into account that, in contrast to non-essential chemical substances, there is a (lower) level of intake below which risk of deficiency conditions or sub-optimal functioning arises."

Guidelines of the SCF (taken over by EFSA) for the development of tolerable upper intake levels for vitamins and minerals, 2000/2006

Definitions

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"**Tolerable upper intake level (UL)** - the maximum level of total chronic daily intake of a nutrient (from all sources) judged to be unlikely to pose a risk of adverse health effects to humans.

'Tolerable intake' in this context connotes what is physiologically tolerable and is a scientific judgement as determined by assessment of risk, i.e. the probability of an adverse effect occurring at some specified level of exposure. ULs may be derived for various lifestage groups in the population."

Definitions

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Adverse effect - change in morphology, physiology, growth, development or life span of an organism which results in impairment of functional capacity or impairment of capacity to compensate for additional stress or increase in susceptibility to the harmful effects of other environmental influences (WHO, 1994). Decisions on whether or not any effect is adverse require expert judgement.

Principles for scientific risk assessment

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The process of the risk assessment may be divided into a number of steps

- Step 1. Hazard identification
- Step 2. Hazard characterisation
- Step 3. Exposure assessment
- Step 4. Risk characterisation

Hazard Identification

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Identification of the adverse health effects that have been demonstrated to be caused by the nutrient.

Human studies provide the most relevant data for hazard identification. Other studies with animals or *in vitro* to be considered

Hazard Characterisation

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The qualitative and quantitative evaluation of the nature of the adverse effects associated with a nutrient; this includes a dose response assessment, i.e. determining the relationship between nutrient intake (dose) and adverse effect (in terms of frequency and severity).

Level at which a nutrient causes adverse effects

Hazard Characterisation

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- Most appropriate/critical data selection
- Identification of NOAEL (highest intake of a nutrient at which no adverse effects have been observed or LOAEL (lowest intake at which an adverse effect has been demonstrated)
- Uncertainty factors (UF)

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Derivation of Upper Tolerable Level (UL)

Derivation of Upper Tolerable Level (UL)

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$$UL = \frac{NOAEL \text{ or } LOAEL}{\text{Total Product of Ufs}}$$

Selection of UF is critical to consider potential effects for nutritional deficiency and excess.

Exposure Assessment

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Evaluation of the distribution of usual total daily nutrient intakes among members of the general population

- All food sources, including water.
- In the EU food supplements are regulated as foods
- Quality of nutrient intake data is very important

Risk Characterisation

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- description of the scientific uncertainties associated with the UL estimates
- Indication of the degree of scientific confidence that can be placed in these estimates
- estimation of intake for population groups
- indication of the margin between recommended or actual intakes and the UL
- where UL cannot be established an indication should be given on the highest level of intake where there is reasonable confidence in data on the absence of adverse effects.

Upper Levels By SCF/EFSA

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Vitamins	Adult Upper Level
Vitamin A	3000 µg
ß Carotene	not est.
Vitamin D	100 µg
Vitamin E	300 mg
Vitamin K	not est.
Vitamin C	not est.
Thiamin	not est.
Riboflavin	not est.
Niacin	10 mg free nicotinic acid / 900 mg nicotinamide
Vitamin B6	25 mg
Folacin	1000 µg
Vitamin B12	not est.
Biotin	not est.
Pantothenic acid	not est.

(not est. = not established)

Upper Levels By SCF/EFSA

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Minerals	Adult Upper Level
Boron	10 mg
Calcium	2500 mg
Chromium	not est.
Copper	5 mg
Fluoride	7 mg
Magnesium	250[a] mg
Iodine	600µg
Iron	not est.
Selenium	300µg
Molybdenum	600 µg

(not est. = not established)
[a] Supplemental readily dissociable salts

Upper Levels By SCF/EFSA

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Minerals	Adult Upper Level
Potassium	not est.
Phosphorus	not est.
Manganese	not est.
Zinc	25 mg
Silicon	not est.
Vanadium	not est.
Tin	not est.
Chloride	not est.
Sodium	not est.
Nickel	not est.

(not est. = not established)

Characteristics of Upper levels (ULs)

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<u>Uls</u> are:

- Based on scientific risk assessment's assumptions and uncertainties
- Not only safe, but safe by a comfortable margin
- Defined and identified to reflect safety of chronic intakes
- Values that take account of identified sensitive populations

Uls are not:

- Thresholds for adverse effects
- "Safety limits"
- Applicable to temporarily elevated intakes

Fundamental principle of Food Law
Risk Analysis

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- Risk Assessment-by risk assessor (scientific advisory body)
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Criteria for establishing maximum amounts of vitamins and minerals

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Safety is the basis for setting of maximum amounts

- Upper safe levels of vitamins and minerals established by scientific risk assessment based on generally accepted scientific data, taking into account, as appropriate, the varying degrees of sensitivity of different consumer groups;
- Intake of vitamins and minerals from all dietary sources
- Due account to be taken of Reference Intakes of vitamins and minerals for the population (Recommended Daily Allowances (RDA) or Population Reference Intakes (PRI)).

Risk Assessment ➔ Risk management

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A model considered:
Quantitative risk categorisation for nutrients with a UL
Using appropriate data on:

- UL as set by SCF/EFSA and other risk assessments
- RDA as set by EU Regulation No 1169/2011
- Mean Highest Intake from food (MHI)
  (i.e. the 97.5 percentile intake of the average male adult)
- The estimated intake from water (IW)

Categorisation of nutrients according to risk using a formula as below and selecting a cut-off point for the PSI:

$$\textbf{Population Safety Index (PSI)} = \frac{\textbf{UL} - (\textbf{MHI} + \textbf{IW})}{\textbf{RDA}}$$

Risk categorisation of vitamins and minerals

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Group 1 No evidence of risk within ranges currently consumed; does not represent a risk to human health

Group 2 Low risk of exceeding the UL

Group 3 Potential risk at excessive intakes

GROUP 1: Nutrients that do not represent a risk to human health

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No SCF/EFSA UL available; based on a qualitative risk categorisation

Vitamin B_1, Vitamin B_2, Biotin, Vitamin B_{12}, Pantothenic acid, Vitamin K, Chromium (based on sources approved for use)

GROUP 1

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- Absence of risk-No scientific rationale for applying risk management measures
- No maximum levels required
- Guidance levels based on Highest Observed Intake (HOI) risk assessment method (FAO/WHO 2006) ???

GROUP 2: Low risk of exceeding the UL

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based on quantitative risk categorisation —PSI based

Vitamin B_6
Vitamin C
Vitamin D
Vitamin E
Folic acid
Nicotinamide
Phosphorus
Magnesium
Molybdenum
Selenium
Potassium†
†Based on qualitative information

GROUP 3: Potential risk at excessive intakes

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based on quantitative risk categorisation-PSI based

Vitamin A
Beta-carotene (smokers)†
Calcium
Copper
Fluoride
Iodide
Iron
Manganese†
Zinc

†Based on qualitative information

Thank you
for your attention