codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 9 **CX/NFSDU 02/9**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON NUTRITION AND FOODS FOR SPECIAL DIETARY USES
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DISCUSSION PAPER ON THE PROGRESS OF WORK BY FAO/WHO AND NATIONAL SCIENTIFIC BODIES IN RELATION TO RISK-BASED APPROACH FOR THE ESTABLISHMENT OF UPPER LIMITS FOR NUTRIENTS

Prepared by FAO

1. The Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU) had been considering the Proposed Draft Guidelines on Vitamin and Mineral Supplements since 1988 when "Several delegations" proposed work in the area of food supplements as part of an overall review of the work of Codex in the area of nutrition.

2. The 20th Session of the CCNFSDU (1996) submitted the Proposed Draft Guidelines to the Codex Commission (CAC) for adoption at Step 5, however the 21st Session of the CAC (June 1997) returned the document to the Committee for re-drafting due to lack of consensus on the content of the guidelines.

3. Further discussions at 21st, 22nd and 23rd sessions at the Committee level with minimal progress. The major unresolved issues: the maximum levels of vitamins and minerals to be contained in supplements and the basis for their establishment.

4. The last 23rd Session of the Committee (November 2001) had considered the Discussion paper on the Application of Methodology of Risk Assessment for Nutrient Issues: the Incorporation of Nutrient Risk Assessment in a Risk-Based Approach to Assist Decision-Making Process of CCNFSDU (CF/NFSDU 01/9). Following the intervention by the Delegation of Australia related to risk-based approaches being followed by several countries at the national level to establish safe upper levels of consumption for vitamins and minerals, the Committee requested FAO/WHO to extend their current work on recommended nutrient intakes to include upper levels (ULs) for vitamins and minerals.

5. At the 23rd Session in Berlin (26-30 November 2001) the Representative from FAO informed the Codex Committee on NFDSU that a follow-up meeting to the Expert Consultation on vitamins and minerals held in Bangkok in 1998 has been actively considered by FAO. The follow-up Expert Consultation would specifically deal with a few vitamins and minerals where new scientific evidence had emerged.

6. It was suggested that the remit of this new expert group would be widened to consider the possibility of looking into the issue of ULs and matters of safety with regard to micronutrient intakes using a risk-based approach. The Observer from the EC informed the Codex Committee that the Scientific Committee for Food had started work on the establishment of ULs for vitamins and minerals. The EC Observer cautioned that this was a long-term exercise and that an international consultation called by FAO/WHO may be able to address this question.

7. Support was also forthcoming based on the experiences in the evaluation of safety of vitamins and minerals by several national and international bodies including manufacturers, producers and consumer groups in developing recommendations based on scientific approaches. The organisations involved in this activity included examples such as the US Institute of Medicine, French Ministries, UK Department of Health, Nordic Council, the EC's Scientific Committee on Food (SCF), Council for Responsible Nutrition (CRN), International Programme on Chemical Safety (IPCS), European Federation of Health Product Manufacturers Association (EHPM) and Consumers for Health Choice (CHC) among others.

8. It was decided that the Committee should be informed at its next session on the progress made in furthering this recommendation of the Codex Committee.

9. Soon after the meeting of the Codex Committee on NFDSU, the Report of the 1998 Bangkok Expert Consultation on Vitamins and Minerals was posted on the FAO's website. Hard copies of the Report were also published although this was considered a preliminary report since the responsibility for publication of the Report was undertaken by WHO as part of WHO's Technical Report Series. Until the availability of this definitive report by WHO the preliminary report published by FAO will be used widely.

10. Developments and scientific advances in several areas related to vitamins and minerals has prompted FAO to consider calling specialized small expert groups to update information related to some of the vitamins (e.g. Vitamin A) and minerals (e.g. iron, calcium). The nature of these meetings are being discussed at FAO and it is likely that the meetings would be convened during the year 2003. At these meetings in addition to dealing with the advances in scientific information related to these specific vitamins and minerals, the experts would also consider ULs and make recommendations on a case by case basis.

11. It is the decision of FAO, after considerable deliberation, that at the outset the Organisation would produce a generic Technical Report outlining the general principles to be adopted in approaching this topic of ULs and safety of specific vitamins and minerals to be undertaken on a case by case basis over the next several years.

12. The approach to be followed would be the one laid out in the proposed draft working principles for risk analysis for application in the framework of the Codex Alimentaris (Appendix II, ALINORM 03/33) with the responsibility for risk assessment being the responsibility of the FAO/WHO Expert bodies and Consultations (risk assessors). According to these working principles, risk assessment should be based on all the available scientific data; predominantly quantitative but also takes into account qualitative information. The need to obtain information wherever possible from developing countries and based on realistic exposure scenarios is also emphasised.

13. The FAO/WHO joint expert consultation report on Human Vitamin and Mineral Requirements provides clarification on a number of the terms used that may be useful in further consideration of the proposed draft Guidelines on Vitamin and Mineral Supplements. The following definitions are quoted from the above report (see Annex).

Annex

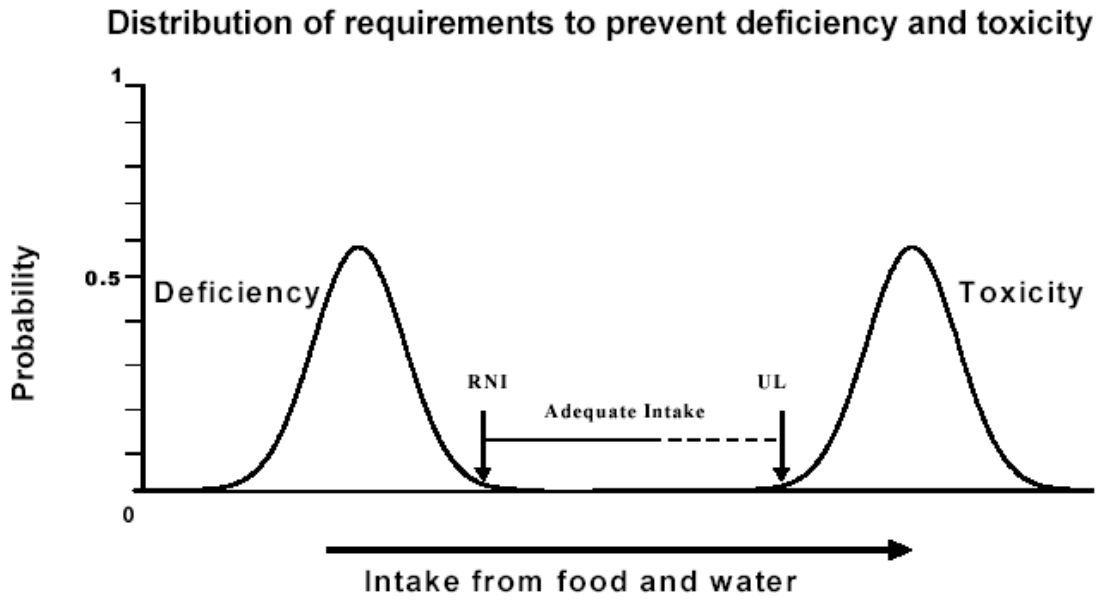
REPORT OF A JOINT FAO/WHO EXPERT CONSULTATION ON HUMAN VITAMIN AND MINERAL REQUIREMENTS, ROME (2002)

Definitions of terms used in the Report

The following definitions relate to the nutrient intake from food (including water) that is required to prevent deficiency conditions. Upper limits of nutrient intake are defined for specific vitamins and minerals where there is a potential problem with excess.

Requirement

A requirement is an intake level, which will meet specified criteria of adequacy, preventing risk of deficit or excess. These criteria include a gradient of biological effects related to the nutrient intake. This dose response will be assumed to have a Gaussian distribution unless it is known to be otherwise. A risk function (a probability of 0 to 1) of deficiency and excess can be derived (***Figure***).



The relevance of the biological effects starts with the most extreme case, that is, the prevention of death. For nutrients where sufficient data on mortality are not available, the nutrient intake that prevents clinical disease or sub-clinical pathological conditions, identified by biochemical or functional assays, is used. The next sets of biomarkers that are used to define requirements include measures of nutrient stores or critical tissue pools. Intakes to assure replete body stores are important when deficiency conditions are highly prevalent. Presently, approaches to define requirements of most nutrients use several criteria examined in combination, functional assays of sub-clinical conditions are considered the most relevant.These biomarkers ideally should be sensitive to changes in nutritional state while at the same time be specific in terms of identifying sub-clinical deficiency conditions. The use of nutrient balance to define requirements has been avoided whenever possible. However, in the

absence of other criteria it has been used. In most cases, balance based on input-output measurements are greatly influenced by level of intake, that is, subjects adjust to high intakes by increasing output, conversely they lower output when intake is low. Thus, if sufficient time is provided balance can be achieved at multiple levels of intake. The same can be said of nutrient blood levels, they usually will reflect level of intake and absorption rather than functional state. Unless balance or plasma level is related to abnormal function or disease conditions, they are inadequate for use as a criteria to support the definition of requirements. Where relevant, requirement estimates should include allowance for variations in bio-availability.

Recommended nutrient intake

Recommended nutrient intake (RNI) is the daily intake, which meets the nutrient requirements of almost all (97.5 percent) apparently healthy individuals in an age and sex specific population group. Daily intake corresponds to the average over a period of time.

Criteria to establish requirements used in this report will be nutrient specific. The estimation of RNI starts with the definition of the criteria for requirement and adds corrections for physiologic and dietary factors. The average requirement value obtained from a group of individuals is then adjusted for inter-individual variability. If the distribution of values is not known, a Gaussian distribution is assumed, that is, a mean plus 2 SD is expected to cover 97.5 percent of the population. If the SD is not known, a value based on each nutrient's physiology is used. In most cases a variation in the range of 10-12.5 percent was assumed; exceptions are noted within chapters. The definition of RNI used in this report is equivalent to that of recommended dietary allowance (RDA) as used by the Food and Nutrition Board of the US National Academy of Sciences (*1*).

Apparently healthy

Apparently healthy refers to the absence of disease based on clinical signs and symptoms and function, normally assessed by routine laboratory methods and physical evaluation.

Upper tolerable nutrient intake level

Upper tolerable nutrient intake levels (ULs) have been defined for some nutrients. ULs are the maximum intake from food that is unlikely to pose risk of adverse health effects from excess in almost all (97.5 percent) apparently healthy individuals in an age and sex-specific population group. ULs should be based on long-term exposure from food, including fortified food products. For most nutrients no adverse effects are anticipated when they are consumed as foods, because their absorption and or excretion are regulated. The special situation of consumption of nutritional supplements which when added to the nutrient intake from food may exceed the UL will be addressed in the specific chapters. The ULs as presented here do not meet the strict definition of no observed effect level used in health risk assessment by toxicologists because in most cases a dose-response curve for risk from total exposure to a nutrient will not be available. For more details on how to derive ULs, see the model presented in Nutrition Reviews (2).

The range of intakes encompassed by the RNI and UL should be considered sufficient to prevent deficiency while avoiding toxicity. If no UL can be derived from experimental or observational data in humans, the UL can be defined from available data on upper range of observed dietary intake of apparently healthy populations.

Protective nutrient intake

The concept of protective nutrient intake has been introduced in some cases to refer to an amount greater than the RNI, which may be protective against a specified health or nutritional risk of public health relevance (e.g., vitamin C intake with a meal to promote iron absorption or folic acid to lower the risk of neural tube defects). The text will indicate when existing data provide justifiable differences between RNI values and protective intake levels. These intakes are expressed as a daily value or as an amount to be consumed within a meal.

References

1. **Food and Nutrition Board, Institute of Medicine**. 1997. *Dietary Reference Intakes*: Washington, DC, National Academy Press.
2. **Anonymous**. 1997. A Model for the Development of Tolerable Upper Intake Levels. *Nutr. Revs.*, 55: 342-351.