Comment by
Council for Responsible Nutrition
Washington, DC USA

The Council for Responsible Nutrition (CRN) offers the following comments on the "Discussion Paper on the setting of maximum and minimum amounts for vitamins and minerals in foodstuffs," dated June 2006. CRN is pleased by the open and responsible procedure of allowing input by all interested parties through provision of a Discussion Paper with adequate review time before comments are due.

CRN is a trade association that represents approximately 75 companies who manufacture food (dietary) supplement ingredients and products. Although we are based in the United States, CRN has official Non-Governmental Organization (NGO) status with the Codex Alimentarius Commission, we have several member companies with home offices in Europe, and several of our US-based companies do business in Europe as well as in other regions. Clearly, we have an intense interest in the regulations that are developed by the European Commission.

Under these circumstances we offer the following comments intended to refine and improve the focus of the Discussion Paper.

General comments:
CRN considers the text of the Discussion Paper to be generally appropriate, and our concerns are much more directed to issues that are omitted or minimally discussed rather than to misdirected content. Because much of the content is quite appropriate, we will comments only on those areas for which we see the need for further elaboration or have some concern.

Specific comments:

- Para 11 and 27:
    - OSL-HOI for some nutrients. Annex I covers only "essential nutrients" but not all have UL values established by the EC SCF/EFSA. For example, there is no EU UL for thiamin, riboflavin, biotin, pantothenic acid, and vitamin B12. This absence of a UL value has led to arbitrarily restrictive policies (French decree: J. Officiel de la Republique Francaise, 28 Mai 2006, Texte 7 sur 62) or discussion policy options (Germany discussion document: BfR—Use of Vitamins in Foods, Toxicological and nutritional-physiological aspects, Part 1) for vitamin B12. Ironically, the absence of a UL for B12 has led to policy or options, when expressed as multiples of the RDA, that are more restrictive for this vitamin, which has no known toxicity by any route of administration despite substantial clinical use at intakes up to thousands of time the RDA, than for pyridoxine which has well established toxicity at sufficiently high intakes. Specifically, the SCF UL for pyridoxine is 25 mg, approximately 15x the RDA, but the German proposal for B12 is 3x the RDA (9 µg) and the French decree is 1x the RDA (3 µg). In terms of consumer protection, we consider something very basic to be wrong in the scientific

policy and methods when the proposed limit is more restrictive for B12 than for pyridoxine.

For nutrients with no known toxicity, the scientific procedure that is missing from the EC FSD and the SCF/EFSA risk assessment method is one that could identify the intake level with sufficient data to establish a lack of toxicity. Fortunately, such a procedure is now available. It was described as the Highest Observed Intake (with adequate evidence of lack of toxicity) in the FAO/WHO report but it was not applied to specific nutrients in this report. This procedure was used but not named by the UK EVM to identify an "advisory level" of 2,000 μg for vitamin B12.

Also, this procedure has been described and applied to nutrients not included in Annex I (series of peer-reviewed articles—Hathcock and Shao/Shao and Hathcock, in Regulatory Toxicology and Pharmacology, 2006).

- Para 17:
  - Article 5 does not specify the source of the UL values to be used by the EC in setting maximums. Although is logical that SCF/EFSA values would be the first choice, the EC should consider other authoritative sources when there are dramatic differences in the values, and justify the choice among the authoritative UL values. This issue is particularly acute for pyridoxine and a few of the minerals, e.g., manganese and iron.
- Para 17, Sub-para 2, and Para 18, Sub-para 4:
  - The Codex guideline adopts but restricts Article 5, para 2 of the FSD. The EC should note that the Codex VM FS guideline is more restrictive than the FSD in the process of giving "due account" to consideration of PRIs when setting maximums through RA. Specifically, the Codex guideline prohibits the setting of maximums solely on the basis of the PRI values. The maximums to be developed by the EC should recognize this restriction in Codex and thus help its member states avoid violation of the Codex guideline.
- Para 11:
  - Annex II needs to be updated based on human clinical trial evidence (e.g., selenized yeast and Se-met, CrPic, etc.)
- Paras. 14, 17:
  - Sum of CF, FF, and DS is the right approach, but extreme percentiles in all categories are not realistic for the high-consumers, and limits consumer choice for the majority.
- Paras. 13, 14:
  - Member states have different food intake patterns, and hence the accounting for dietary intakes must differ. To provide consumer protection but at the same time to prevent unnecessary restrictions to the circulation of products within the EU member states, the maximums identified by the EC should be based on an EC-wide uniform set of UL values (for total intakes from all sources, for all nutrients but a few specified exceptions) and similarly an EC-wide set of percentiles to be applied to the food intake survey data for each member state.

- Para 18—same comments as for Para 17.
- Paras. 17 1(a) and 18 3(a):
    - Consideration of the different sensitivities among subpopulations is appropriate, but its emotional appeal sometimes overrides common sense and practicability. In properly conducted risk assessment, consideration of differing sensitivities should have been included, although examination of the entire collection of UL publications reveals uneven application of this rule.

      Consideration of different sensitivities often cannot include the most sensitive subpopulation without causing more have for the majority than protection for the sensitive subpopulation. For example, zinc limits high enough (several hundred milligrams) to allow nutritional adequacy for the few with acrodermititis enteropathica would allow levels toxic to the majority. Conversely, copper levels low enough to protect those with Wilson's disease would cause deficiency in the large majority.

      Although is it not an issue at this time with the FSD implementation including only vitamins and minerals, persons with phenylketonuria or hemachromatosis provide another example of subpopulations that must not be the basis for policy directed toward the overall population.
- Para 28:
    - First question—If the absence of a UL is due to extremely low (unknown) toxicity, the EC should apply the FAO/WHO Highest Observed Intake (HOI) method (A model for establishing upper levels of intake for nutrients and related substances; Report of a Joint FAOWHO Technical Workshop on Nutrient Risk Assessment, FAO/WHO 2006), and apply this type of risk assessment in the maximums procedure of Article 5. Of course, it may be necessary for the EC to request that EFSA identify the actual HOI values for nutrients with no established toxicity. If there is established toxicity but nonetheless the SCF/EFSA has not set a UL because of poor dose-response data, the EC should look to the IOM and EVM for values that may be applied to establish maximums.
    - Second question—Yes, there is reason to set maximum values for these nutrients. The responses of Germany and France on vitamin B12 illustrate the unnecessary and unjustified restrictions that governments may impose if the UL method is not extended to include a HOI value where the scientific data justify it.
    - Third question—the simultaneous regulation of maximums for supplements and fortified foods issue poses a problem of equitable division of the total maximum between the categories that has no scientific answer. Similarly, the concurrent availability of multiple products within each of those categories again poses the same difficulties in relation to the multiple products within each category. The answers to the relative amounts of the UL allocated to supplements and to fortified foods and to each of the multiple products within each of those categories must be a practical, not scientific.

Extreme assumptions are inappropriate and give counterproductive answers. Within the supplement category or the fortified foods category, the EC should not make any of the following assumptions because they are generally invalid:

- that only one product in each category will be consumed
- that every available product in that category will be consumed
- that the logical allocation for supplements and fortified foods is equal
- that future fortification practices or supplementation trends can be predicted and accommodated in the maximums set

- Para 33:
  - First question—CRN (US) has no data for Europe.
  - Second question—a panel of European nutrition researchers with knowledge of the surveys in different countries and regions could advise on the typical content of regional diets (Nordic? Mediterranean? Ireland-UK? Eastern? Other?)
  - Third question—The intakes by different populations groups needs to be considered, but "worst-case" intakes should not be assumed. The regional patterns mentioned in the previous answer are sufficient.
- Para 42—Question: The overall thrust of Article 5 is that maximums are to be set on the basis of risk assessment, and that "due account" to PRI values is to be given while utilizing risk assessment. Clearly, it is not the intent of Article 5 that maximums should be based on PRIs instead of risk assessment. Moreover, the additional sentence incorporated into the Codex VM FS guideline (CAC/GL 56-2005) makes it clear that any maximum based sole (i.e., directly) on the PRI would be a violation of Codex, and thus WTO obligations. *Ver batim*, the Codex guideline states in relation to giving due account to population reference intakes that "This provision should not lead to setting of maximum levels that are based solely on recommended nutrient intakes (e.g. Population Reference Intake or Recommended Dietary Allowance)."

  The best available proposal for giving "due account" to the PRI while setting maximums under Article 5 is provided in the ERNA/EHPM Risk Management Model. This method takes into account the PRI and current intake sources as denomination of UL ÷ PRI to categorize the nutrients into different risk categories.

  The "nutritional dimension" mentioned in the French Annex to this proposal is not included in Article 5. Clearly, the EU FSD envisions that nutritional needs be assured by availability of appropriate products, sufficient family economic resources, and guidance by nutrition labeling. The only purpose of the maximums provisions in the FSD and the Codex guideline is to assure consumer safety in relation to fortified products and high-potency supplements.

- Para 46
  - First question—yes, the amounts should be the same if the purpose of the addition is to provide the nutrient but not if the nutrient source is added for another purpose (e.g., ascorbic acid added to protect the product against oxidation). Minimum amounts help assure the consumer of receiving a significant amount of the nutrient if the addition is intentional and the amount

identified on the label. Without minimums, the consumer might have to consume several products to obtain amounts of the nutrients that would provide health benefits.

- Second question—The nutritionally significant minimums would be approximately the same as the amounts that would trigger labeling requirements. For convenience, they should be set at the same levels.