

02/08/2007

Comments from the European Community on

Codex Circular Letter CL 2007/18-FBT:

Proposed Draft Annex to the Codex Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA:

Food Safety Assessment of Foods derived from Recombinant-DNA Plants modified for Nutritional or Health Benefits

**European Community Competence
European Community Vote**

The European Community (EC) welcomes the outcome of the meeting of the physical working group (WG) on Foods Derived from rDNA Plants Modified for Nutritional or Health Benefits which was established by a decision of the Codex *ad hoc* Intergovernmental Task Force on Foods Derived from Biotechnology during its 6th Session.

The WG was given the mandate to draft an Annex to the Codex Plant Guidelines¹ on the basis of a scoping paper that was circulated within an electronic working group (open to all Codex Task Force members and observers) and the subsequent comments received (contained in documents CX/FBT 06/6/5 and CX/FBT 06/6/5-Add.1), as well as on the basis of the comments provided during the 6th Session.

The WG took place in Ottawa, Canada, between the 7th and the 9th of May. The EC would like to thank the pro-active role played by Canada as chair of the group and Argentina and New Zealand as co-chairs.

Substantial progress has been made on the definition of the general approach of the Annex to the Codex Plant Guideline. In particular it is important to recall that general guidance for the safety assessment of foods derived from recombinant-DNA plants is already provided by the existing Codex Plant Guideline. The aim of the Annex is thus to focus on the safety assessment of foods derived from GM plants modified for nutritional or health benefits providing additional guidance.

The Annex does not extend beyond safety assessment, and risk management issues² and the assessment of the benefits or any corresponding health claims were therefore not considered within the scope of the document.

¹ Codex Guideline for the Food Safety Assessment of Foods derived from Recombinant-DNA plants (CAC/GL 45-2003)

² Post-market monitoring is covered by paragraph 20 of the Codex principles (CAC/GL 44-2003) and by paragraph 6 of the Codex Plant guideline, specifically with reference to monitoring changes in nutrient intake levels, associated with the introduction of foods likely to significantly alter nutritional status and to determine their human health impact.

The EC would like to confirm the point already raised during the WG in Ottawa on the need to establish some guidance for the assessment of the benefits of foods derived from rDNA plants modified for nutritional or health benefits. The EC is of the view that a careful consideration of the benefits needs to be done in order to evaluate the overall impact of the above-referred food. The evaluation of potential benefits of a product in a given population should be made by the respective competent national authorities in the country where the product should be placed on the market. The EC is of the view that further consideration should be given by Codex on the way to establish these benefits. If this question can not be considered by this Task Force, it could be carried out by the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU). This request will be reiterated at the Codex Task Force meeting at its 7th session in Chiba.

The other main issues are particularly relevant for the EC: the importance of having clear definitions, the need for different approaches for the safety assessment of nutrients (based on tolerable intake levels) and related or undesirable substances (based on for instance ADIs), and the need for more guidance, for instance as regards the choice of the appropriate comparator and the design of animal studies.

As regards the importance of the need of clear definitions, no consensus was reached on the definition of “related substances”, and the drafting of this definition (and other definitions, such as “tolerable upper intake level”) was therefore deferred to the CCNFSDU (which is however an unfortunate outcome of the WG given that definitions are key for the understanding of the guidelines under discussion). We are of the view that this issue needs to be discussed once again in the context of the 7th session of the Task Force.

The importance of the choice of the appropriate comparator for these kinds of products was recognised within the comparative assessment approach, and was subsequently highlighted in the Annex.

The need for animal feeding studies is covered by paragraph 53 of the Codex Plant guideline. Most delegates were of the opinion that this paragraph provides sufficient guidance on animal feeding studies, and that additional guidance would only be acceptable if it would be specific to foods derived from GM plants modified for nutritional or health benefits. In this framework the EC has proposed a paragraph specifying that, in the case animal studies are performed to assess the nutritional value and the bioavailability of the newly expressed substance(s), special attention needs to be paid to the sensitivity of the animal species to the nutrient(s) or substances(s) in question, and to the formulation of control diets, including the possibility of external fortification of the appropriate comparator.

The paragraph was briefly discussed, and given that no consensus could be reached, will again be open for discussion at the 7th session of the Codex Task Force meeting. The EC is of the opinion that the concept formulated in the current form of the paragraph should be kept in the final version of the annex.

Please find below some more specific comments concerning the draft text:

Section 1 - Introduction:

Paragraph 2

The three bullet points in subparagraph b) should take into account the fact that some substances may be expressed for the first time by the plants, such as vitamin A in Golden Rice.

Section 2 - Definition:

Since both terms “nutrient” and “related substance” are used in the Annex we consider a definition of “related substance” necessary. We suggest adding the following definition that is in line with the definition in the Report of the Joint FAO/WHO Technical Workshop on Nutrient Risk Assessment, Geneva, Switzerland, 2-6 May, 2005:

“Related substances are inherent constituents of food that have a favourable impact on health but which do not fulfil the definition for ‘nutrient’ according to b) and c) above”.

Section 3 – Food Safety Assessment:

Paragraph 5

The reference between brackets to “Codex Plant Guideline paragraph 4 and 51” would be more logic to follow the first sentence of paragraph 5 as the Codex Plant Guideline elaborates on the comparative approach and the conventional counterpart for recombinant-DNA plants in general. The sentence that follows the first sentence of paragraph 5 further stress the importance of the choice of the appropriate comparator for the assessment of recombinant-DNA plants modified for nutritional or health benefits.

The revised paragraph would read as follows:

“Rather than trying to identify every hazard associated with a particular food, the intention of a safety assessment of food derived from recombinant-DNA plants is the identification of new or altered hazards relative to the conventional counterpart (**Codex Plant Guideline paragraph 4 and 51**). Since recombinant-DNA plants modified for nutritional or health benefits result in food products with a composition that may be significantly different from their conventional counterparts, the choice of an appropriate comparator is of great importance for the safety assessment addressed in this annex. Those alterations identified in a plant modified to obtain nutritional or health benefits are the subject of this safety assessment.”

Paragraph 6

For clarity we suggest to delete the words “have been”. The amended sentence would read:

“Upper levels of intake for many **nutrients set out** by some national, regional and international bodies may be considered, as appropriate.”

Paragraph 8

We suggest replacing the word “resulting” by “expected or foreseeable”. The amended sentence would read:

“Although it is preferable to use a scientifically-determined upper level of intake of a specific nutrient or related substance, when no such value has been determined, consideration may be given to an established history of safe use for nutrients or related substances that are

consumed in the diet if the **expected or foreseeable** exposure would be consistent with those historical safe levels.

Paragraphs 9 and 10

As a general remark, we suggest changing the order of the two paragraphs because paragraph 10 provides an introduction to the following paragraphs on bioavailability.

Regardless of this suggestion, we propose to remove the square brackets in the first sentence of the current paragraph 9, thus keeping the term “chemical form”. For the sake of clarity, the word “nutrient” should be inserted before “added at controlled concentrations”. In addition, a reference should be made to the examples in attachment 2. In the second sentence, we suggest to delete either the word “levels” or, preferably, the word “concentration” in order to avoid duplication. The bracketed words in the third and fourth sentences should be replaced by “different chemical forms”. The alternative term “analogue” describes a similar substance but not different forms of the same substance, such as listed in the attachment 2. The term “different” covers the case of multiple forms as well as many or few different forms of nutrients or other substances contained in the food. For improvement of clarity, in the fourth sentence (last line of para 9) the words “their combined bioavailability” should be replaced by “the total bioavailability of the nutrient or related substance”.

The revised current paragraph 9 would read as follows:

“With conventional fortification of food, typically the **chemical form** of a nutrient³ or related substance is characterized and **the nutrient is** added at controlled concentrations. **Levels** of plant nutrients or related substances may vary in both conventionally bred and recombinant-DNA plants due to growing conditions. In addition, **different chemical forms** of the nutrient that may not be characterized from a nutrition perspective might be expressed in the food as a result of the modification. Where appropriate, information may be needed on the **different chemical forms** of the nutrient(s) or related substance(s) expressed in the portion of the plant intended for food use, their respective levels and the **total bioavailability of the nutrient or related substance** in the food.”

Paragraph 11

The first and second sentences should be corrected as follows:

“Bioavailability will vary for different nutrients, and **regimes of testing for availability** should be relevant to the nutrient ...”

“In vitro, and in vivo **methods to determine bioavailability exist**, the latter ...”

Paragraph 12

To improve clarity, the wording of the paragraph should be further modified as follows:

When animal studies are performed to **assess the bioavailability** of a **substance(s), an important criterion for the choice of the animal species (strain/sex) is its sensitivity towards the substance in question. For the assessment of the nutritional value and/or the bioavailability of newly expressed substances** the control diets need to be formulated in

³ See Attachment 2

such a way that the **key endpoints measured** are responsive to a difference in the quantity and/or bioavailability of the enhanced nutrient(s), substance(s), or decreased undesirable substance(s). In the case of a new or increased level of a nutrient(s) or related substance(s), the choices for control diets may be made on a case-by-case basis and **an** appropriate comparator(s) with and without external fortification may be necessary.

Paragraph 13

We suggest replacing of the word “impact” in the second sentence by the word “influence”. The respective part of the sentence would read:

“In the context ...any known factors that **influence** bioavailability.”

Paragraph 14

We suggest to carefully consider the wording of this paragraph in order to better specify its meaning.