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Agenda Item 5

CX/FBT 07/7/5  
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**JOINT FAO/WHO FOOD STANDARDS PROGRAMME**  
**CODEX AD HOC INTERGOVERNMENTAL TASK FORCE**  
**ON FOODS DERIVED FROM BIOTECHNOLOGY**

*Seventh Session*

*Chiba, Japan, 24 – 28 September 2007*

**PROPOSED DRAFT ANNEX TO THE GUIDELINE FOR THE CONDUCT OF FOOD SAFETY ASSESSMENT OF FOODS DERIVED FROM RECOMBINANT-DNA PLANTS: *FOOD SAFETY ASSESSMENT OF FOODS DERIVED FROM RECOMBINANT-DNA PLANTS MODIFIED FOR NUTRITIONAL OR HEALTH BENEFITS AT STEP 4***

Comments at Step 3, in response to Circular Letter CL 2007/18-FBT,  
by Australia, Brazil, European Community, Kenya, Malaysia, New Zealand, Philippines, BIO and ILSI

## **AUSTRALIA**

Australia would like to express its appreciation to the Working Group and its Chair and co-Chairs for their work in developing the proposed draft annex and would like to offer the following comments in response to CL 2007/18-FBT.

### **General comments**

Australia agrees that the scope of the proposed draft annex should be limited to the food safety assessment of foods derived from plants modified for nutritional or health benefits and that the proposed annex should not extend to risk management measures or the assessment of benefits. Australia is also strongly supportive of the approach taken by the Working Group to focus on those areas specific to the safety assessment of foods derived from plants modified for nutritional or health benefit and not repeat or revise aspects already addressed in the overarching Plant Guideline.

### **Formatting and Structure**

The report of the Working Group refers to the possible need to revisit the formatting and structure of the proposed draft annex, and in particular the sequential order of the paragraphs. Australia has considered this particular issue and agrees there may be a need to re-order some of the paragraphs. For example, Australia considers that the flow of the document may be improved if paragraph 4 was placed after paragraph 5.

Australia also believes the flow of the document may be improved by revising paragraphs 9 and 10 as follows:

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

Bioavailability of the nutrient(s), related substance(s), or undesirable substance(s) in the food that were the subject of the modification in the recombinant-DNA plant should be established, where appropriate. If [multiple chemical forms/analogues] of the nutrient(s) or related substance(s) are present, their combined bioavailability should be established, where appropriate.

### **Specific Issues**

#### Paragraph 9

This paragraph contains square brackets around the terms “chemical form” and “multiple chemical forms” and an alternative term (“multiple chemical analogues”) is also included. Attachment 2 to the Working Group report provides examples of what is meant by different “chemical forms” of particular nutrients.

Australia finds the term “chemical form” to be clear in terms of its meaning and therefore would prefer to see it retained in preference to “chemical analogue” or “multiple chemical analogue”. Australia would also like to suggest that rather than using the term “multiple chemical forms”, it might make the meaning of paragraph clearer if the term “more than one chemical form” is used. For example (and taking into account the revision already suggested above):

“In addition, more than one chemical form of the nutrient ~~that may not be characterised from a nutrition perspective~~ might be expressed in the food as a result of the modification and these may not be characterised from a nutrition perspective. Where appropriate, information may be needed on the different multiple chemical forms/analogues of the nutrient(s) or related substance(s) expressed in the portion of the plant intended for food use, and their respective levels and their combined bioavailability.

#### Paragraph 12

Australia appreciates the intent behind inclusion of this paragraph in the proposed draft annex however we do not think its inclusion is warranted. We are concerned that this paragraph gives unjustified prominence to animal feeding studies when in fact the preceding paragraph clearly states that human studies may provide more relevant information about whether and to what extent the nutrient or related substance is bioavailable.

We also note that the Plant Guideline already provides adequate guidance regarding the possible use of animal feeding studies (paragraph 53) and also provides general guidance in relation to the conduct of studies intended to develop data for safety assessments (paragraph 20). Australia would therefore propose deletion of this paragraph.

#### Paragraph 14

Australia does not consider it appropriate to include paragraph 14 in the proposed draft annex because it addresses a risk management issue. As agreed by the Working Group, and stated in paragraph 1 of the proposed draft annex, consideration of risk management measures is outside the scope of the document.

Australia also notes that this issue is covered to some extent by paragraph 21 of the Plant Guideline, where it states that the “outcome of the safety assessment process is to define the product under consideration in such a way as to enable risk managers to determine whether any measures are needed and if so to make well-informed and appropriate decisions”. Australia does not believe it would be appropriate for the proposed draft annex to pre-judge or pre-empt such risk management decisions.

### **BRAZIL**

Brazil agrees with proposed report and is for the suppression of the square brackets of paragraphs 9, 12 and 14, adopting their contents as part of the body of the document.

## EUROPEAN COMMUNITY

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 6<sup>th</sup> Session.

The WG was given the mandate to draft an Annex to the Codex Plant Guidelines<sup>1</sup> 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 6<sup>th</sup> Session.

The WG took place in Ottawa, Canada, between the 7<sup>th</sup> and the 9<sup>th</sup> 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 issues<sup>2</sup> and the assessment of the benefits or any corresponding health claims were therefore not considered within the scope of the document.

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 7<sup>th</sup> 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 7<sup>th</sup> 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.

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

<sup>2</sup> 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 paragraph was briefly discussed, and given that no consensus could be reached, will again be open for discussion at the 7<sup>th</sup> 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 nutrient<sup>3</sup> 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 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.

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<sup>3</sup> See Attachment 2

**KENYA**

Kenya commends the working group led by Canada for the good work done in further drafting of the annex by a physical group. Kenya proposes that:

**Paragraph 9**

1. The word “[chemical form] be replaced by fortificant form.
2. Delete the word “multiple chemical forms” in square brackets and retain analogues.

**Paragraph 12**

It should be retained to support paragraph 11, and to provide further guidance in the choice of animal models, and the formulation of control diets for use in animal studies.

**Paragraph 14**

It should be deleted.

The words “nutritional disadvantages” are not part of the scope for this annex.

Nutritional disadvantages will be identified in dietary exposure assessments covered in paragraph 13-17.

**MALAYSIA****General comment**

In terms of the formatting and the structure of the draft annex attached to the working group’s report, Malaysia prefers to have a more complete document that can stand alone without other documents referred.

**Specific comments****ATTACHMENT 1, SECTION 3 – FOOD SAFETY ASSESSMENT****1. Paragraph 9, Pg 5**

Malaysia would like to seek clarification regarding the ‘multiple chemical forms’, whether it referred to only the well-known common nutrients.

Regarding the information on the bioavailability of nutrients in the food, Malaysia would also like to seek clarification whether it is compulsory to include those information.

**2. Paragraph 12, Pg 5**

Malaysia proposes to delete this paragraph as there is already available scientifically accepted protocol to undertake this animal studies.

**3. Paragraph 14, Pg 5**

Malaysia propose to delete this paragraph as this is already covered under paragraph 13.

**NEW ZEALAND**

New Zealand would like to thank the Working Group for its achievements in producing the proposed draft annex. New Zealand supports the approach taken by the working group and generally supports the document, as written in Attachment 1.

New Zealand would like to make the following comments in response to Attachment 1 of CL 2007/18-FBT.

**Section 3 – Food Safety Assessment**

Some delegations considered the term “chemical form” to be unclear and suggested “chemical analogue” instead. In the second and third instance of “chemical form”, in paragraph 9, New Zealand believes that either “chemical form” or “chemical analogue” would be appropriate. However, in the first sentence of paragraph 9, we believe that a term such as “chemical form” or “chemical nature” would be preferable, as the emphasis in this instance should be on the characteristics of the nutrient (eg, oxidation state, isomerism, conjugates etc.) rather than the nutrient itself.

New Zealand agrees with the intent of paragraph 12, and believes that animal studies, where justified, must be properly designed and conducted. We believe that this is adequately covered in paragraphs 14 and 15 of the Principles for the Risk Analysis of Foods Derived From Modern Biotechnology (CAC/GL 44-2003).

New Zealand appreciates the desirability of a modified food not nutritionally disadvantaging consumers when compared with the food it is intended to replace, as noted in paragraph 14. However, New Zealand has two questions regarding this paragraph, as written. Firstly, a categorical statement that a modified food “should not be nutritionally disadvantageous” in this annex to the rDNA plants safety-assessment guideline (CAC/GL 45-2003) appears to blur the distinction between risk assessment and risk management. Secondly, balancing the risk-management needs of different consumers is often a difficult task, complicated by many more factors than regional consumption patterns alone. New Zealand believes that this risk management is an activity best undertaken at the national level.

## PHILIPPINES

### 1. ITEM 6: Scope of the Document

- ◆ Risk Management Measures: The Philippines is of the position that risk management measures and examples of risk management measures be included in the scope of the proposed Draft Annex. In addition, the Philippines wishes to be clarified on the rationale as to why the Working Group agreed that risk management measures were not required under the scope of the Draft Annex.
- ◆ Health Benefits: The Philippines supports the decision of the Working Group that listing of the health benefits should not be included in the proposed Draft Annex.

### 2. ITEM 9: Structure of the Annex

- ◆ The Philippines is of the position that the Proposed Draft Annex be structured as a stand-alone document in order for the document to be presented in a clear, continuous and simple format that minimizes the need for cross-referencing to other documents.

### 3. Assessment of Food Safety Considerations

- ◆ Item 10: Examples of undesirable substances. The Philippines agrees on the position that the examples of toxins, allergens and anti-nutritional factors should not be included in the proposed Draft Annex. We believe that the terms which are contextualized at present, describing “toxin, allergen, and anti-nutritional factors” may change in the future. Thus, we propose that a definition of ‘undesirable’ substances be established within the context of the proposed Draft Annex.
- ◆ Item 11: Definition: The Philippines suggests that the definitions for the following terms as it relates to the proposed Draft Annex, be established by the Working Group in cases where (a) there are no existing definitions; and (b) there are changes or expanding definitions:
  - i. related substances;
  - ii. bioavailability
  - iii. undesirable substances; and
  - iv. upper levels
- ◆ Item 12 and 13: Exposure assessment and Proper Design of Feeding Studies: The Philippines agrees to retain the square brackets in paragraph 12 and 14 of Attachment 1 for further elaboration of its intent and purpose by the Working Group.
- ◆ Item 14: Definition of Multiple Chemical Forms: The Philippines proposes that the Working Group establish a definition of “Multiple Chemical Forms” and supports further elaboration the term in order to provide a clear guidance for countries as to what nutrients may fall under this criterion. In addition, the Philippines suggests inclusion of other examples of nutrients having multiple chemical forms as the current list may not be exhaustive.

**BIO**

On behalf of the Biotechnology Industry Organization, we appreciate the opportunity to provide comment on the above-referenced document at Step 3 of the Codex process, in preparation for a full discussion of the topic during the Seventh Session of the Codex ad hoc Intergovernmental Task Force on Foods Derived from Biotechnology to be held in Chiba Japan in September 2007.

BIO is a not-for-profit trade association that represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States (U.S.) and in 31 other nations. BIO members are involved in the research and development of healthcare, agricultural, industrial and environmental biotechnology products.

We strongly agree that any language and guidance developed to assess the safety of nutritionally enhanced food products developed through or derived from modern biotechnology should closely adhere to the structure developed for the Working Principles for Risk Analysis for Application in the Framework of the Codex Alimentarius.<sup>4</sup> Further, we concur with the assessment of the Working Group that the Annex should be limited to the food safety assessment of foods derived from plants modified for nutritional or health benefits and that risk management measures are outside the scope of the remit of the Working Group.

Should time permit following the completion of this Annex, we would be interested to engage in a dialogue to determine what role Codex might have in characterizing the benefits of modern biotechnology to food safety and consumer protection. However, based on the brief comments in the CL, we do not believe that the WG should undertake this work within the TF at this time.

**Specific comments on the Proposed Draft Annex****Section 1- Introduction**

Para.1- We agree that the document should not cover assessment of the benefits themselves or any corresponding health claims or risk-management measures.

Para.2- factors which determine whether a recombinant-DNA plant is modified for nutritional or health benefit might be included as part of the definition under Section 2.

**Section 3- Food Safety Assessment**

Para.8-We strongly agree that consideration of the 'history of safe use' is appropriate to the assessment of nutritional and health benefit, particularly when ADI are not developed (as in the case of omega 3 fatty acids, for example).

Para.10- The bioavailability of nutrients, whether derived from conventional breeding, fortification of food, or through modern biotechnology would not be expected to differ unless the nutrient itself were chemically different. Under such circumstances, some assessment of the character of the nutrient would support the level of bioavailability of the nutrient when compared with that nutrient from its conventional comparator.

Para.11- See #10 above regarding bioavailability. Appropriate methods for assessment of the chemical nature of specific nutrients exist. Demonstration of bioavailability through *in vitro* testing as well as from published studies should be used to demonstrate equivalence (or lack of equivalence) of nutrients altered for nutritional or health benefit. Animal studies, and in particular, human studies would not typically be necessary in order to demonstrate such benefits. Furthermore, these studies are costly and provide little additional information for the purposes of characterizing 'safety' of the foods. When claims in labeling are made, such differences may be important but would be the subject of a separate assessment for efficacy rather than safety.

Para.12- This Annex is intended to be for the purposes of establishing the food safety of foods enhanced for nutritional or health benefit through modern biotechnology. Discussion of nutritional equivalence, bioavailability and animal models is not appropriate for this work and rather should be referred to the appropriate Codex Committee if it is to be further considered. Design of controlled experiments is beyond the scope of this Annex.

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<sup>4</sup> Codex Alimentarius Commission Procedural Manual, 17<sup>th</sup> edition



Para.13- We strongly agree that most, if not all, aspects of dietary exposure assessment are not unique to recombinant-DNA plants modified for nutritional or health benefits. Therefore, any such discussion of dietary exposure assessment of nutrients either generally or specifically in the context of recombinant-DNA plants should be broadened in scope to be generalized in the context of all foods, and undertaken within the Codex Committee for Nutrition for Special Dietary Uses rather than in this Task Force.

Para.14- We believe this paragraph should be deleted. This element is a risk management function and is thus outside the scope of this work. It is not possible to generalize to global food consumption patterns in order to determine which foods would replace others in an otherwise 'usual' diet.

Para.16- We agree that consumption patterns will vary among countries, and in keeping with the language in this paragraph, further contend that paragraph #14 should be deleted.

Para.17- This paragraph deals with how to conduct the assessment of nutritional efficacy rather than safety. The toxicological assessment is addressed in the Plant Guideline, and comments relating to upper levels and comparators already are addressed in this draft Annex. Further, nutritional assessment methodologies would be addressed in the CCNSFDU and if appropriate by a separate expert assessment. We believe this paragraph is redundant and could be deleted.

## ILSI

The International Life Sciences Institute (ILSI) International Food Biotechnology Committee would like to submit the comments below regarding the draft Annex to the Codex Guideline for the Conduct of Food Safety Assessment of Foods derived from Recombinant-DNA Plants: Food Safety Assessment of Foods Derived from Recombinant-DNA Plants modified for Nutritional or Health Benefit". ILSI also would like to provide information on two ILSI documents<sup>5</sup> regarding nutritional and safety assessments of foods and feeds nutritionally improved through biotechnology.

It is essential that regulatory guidelines be based on sound science using the best critical analysis of available data. The Annex, as written, supports a process approach to safety assessment which does not have a sound scientific foundation.<sup>6</sup>

Comments on the above-mentioned draft Annex are as follows:

- Para. 10: "Bioavailability of the nutrient(s), related substances(s), or undesirable substance(s) in the food that were the subject of the modification in the recombinant-DNA plant should be established, where appropriate."

*Comment:* Although case-by-case specifics should always be considered, typically, bioavailability is assumed to be 100% during a risk assessment. Including guidance for establishing bioavailability is beyond the scope of this annex. Bioavailability is a component of a nutritional assessment and this Annex has clarified that nutritional benefit is not the focus of the safety assessment of plants developed through modern biotechnology. The product not the process should be the focus of regulations and guidelines. Paragraph 11 would also be outside the scope of this Annex since it further elaborates on bioavailability studies.

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<sup>5</sup> ILSI (2004) Nutritional and Safety Assessments of Foods and Feeds Nutritionally Improved through Biotechnology. *Comprehensive Reviews in Food Science and Food Safety*. April, vol 3, p 38-104 (<http://www.ift.org/pdfs/crfsfs/crfsfsv3n2p0035-0104ms20040106.pdf>).

ILSI (2007) Nutritional and Safety Assessments of Foods and Feeds Nutritionally Improved through Biotechnology: Case Studies. International Life Sciences Institute, Washington, D.C. *Pre-publication Draft*.

<sup>6</sup> Bradford KJ, Gutterson N, Parrott W, Van Deynze A, Strauss SH. 2005a. Reply to "Regulatory regimes for transgenic crops." *Nat Biotechnol* 23:787-789;

Bradford KJ, Van Deynze A, Gutterson N, Parrott W, Strauss SH. 2005b. Regulating transgenic crops sensibly: lessons from plant breeding, biotechnology and genomics. *Nat Biotechnol* 23:439-444;

Cellini F, Chesson A, Colquhoun I, Constable A, Davies HV, Engel KH, Gatehouse AM, Karenlampi S, Kok EJ, Leguay JJ, Lehesranta S, Noteborn HP, Pedersen J, Smith M. 2004. Unintended effects and their detection in genetically modified crops. *Food Chem Toxicol* 42:1089-1125;

A.McHughen. 2007. Fatal flaws in agbiotech regulatory policies. *Nature Biotechnology*. 25(7): 725-727.

- Para. 12: Text in brackets relating to controls in animal feeding studies.

*Comment:* There is no scientific basis for providing specific guidance for controls related to improved nutrition crops since controls are important in all analytical methods, not just improved nutrition GM crops. The current Codex Plant Guideline provides adequate discussion of animal feeding studies (paragraphs 10 and 11, pages 8-9). Therefore, providing specific guidance on controls in this Annex gives the inadvertent impression that nutritionally-improved crops have some unique feature warranting additional guidance, which is not the case and which was not supported by many members of the Working Group in Ottawa (hence the square brackets around this paragraph).

- Para. 13: "... Exposure to a nutrient(s) or related substance(s) should be evaluated in the context of the total diet and the assessment should be carried out based on the customary dietary consumption, by the **relevant population(s)**, of the corresponding food that is likely to be displaced. ..."

*Comment:* The term "relevant populations" should be clarified (identified) by inserting a footnote referring to Paragraph 49 of the Codex Plant Guideline. This paragraph identifies **specific** population groups such as infants, children, pregnant and lactating women, the elderly, those with chronic diseases or compromised immune systems.

- Para. 14: Text in brackets stating that nutritionally-improved foods should not be disadvantageous to the consumer compared with the foods intended to be replaced.

*Comment:* This paragraph includes consideration of benefits as well as decisions made during risk management. As stated in paragraph 1 of the Annex, both benefits and risk management are outside of the scope of this Annex.