# codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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**Agenda Item 5** **CX/FBT 06/6/5-Add.1**

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**CODEX AD HOC INTERGOVERNMENTAL TASK FORCE ON FOODS DERIVED FROM BIOTECHNOLOGY**

***Sixth Session***

***Chiba, Japan, 27 November – 1 December 2006***

# PROPOSED DRAFT ANNEX (SCOPING DOCUMENT) 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

***Comments at Step 3 by Argentine, Australia, Costa Rica, European Community, Japan, Kenya, Mexico, New Zealand and the United States of America***

**ARGENTINA**

Argentina would like to compliment the Chair of this electronic working group for an excellent work on reviewing and presenting the diversity of proposals received. Argentina would like to suggest that a final physical meeting is held one day before to the upcoming Task Force 6th Session, so a more refined document can be presented for discussion as a CRD. The detailed observations of Argentina to the current scoping document are listed next (boxes indicate quoted text from CX/FBT 06/6/5).

**• Putative differences in food presentation to the consumer**

> 30. The impact of post-harvest factors such as storage, food processing and home preparation on the stability of the nutrient or related substance were also identified as important elements to consider as their relevance for nutritional or health benefits is dependent upon the levels present when consumed. **In contrast to foods that are conventionally fortified, nutritionally-enhanced plants obtained as a result of genetic modification may be more likely to be presented to the consumer in their raw forms**. As such, the crop to which a new trait is being introduced should be considered in relation with all possible usages in a given population.

Regarding the highlighted phrase of this paragraph (bold format is ours), we do not agree that food products derived from nutritionally-enhanced r-DNA plants will be more likely to be consumed in their raw forms or in different ways from the conventional products. Current examples are not anticipated to be processed differently from their conventional counterpart foods. One of the assets of nutritionally enhanced foods will reside in the possibility of using it as a better alternative to their conventional counterpart food without introducing changes in food processing or manipulation. Finally, Food processing is ruled mostly by practical (e.g. cooking for inactivating anti-nutrients) or cultural reasons, which are not related to the nutritional enhancement.

**• Substances that are not covered**

> **Section 1 – Introduction**
> **- Scope**
>
> *The following factors determine whether an rDNA plant is an rDNA Plant Modified for Nutritional or Health Benefit, and as such within the scope of the Annex:*
> *a) the rDNA plant exhibits a particular trait in a portion of the plant intended for food use, and;*
> *b) the trait aims to **alter** either the quantity or bioavailability of a nutrient or related substance, an anti-nutrient, a toxin or an allergen, or their interactions with other components of the plant, to achieve an intended nutritional or health benefit.*
>
> *The Annex does not cover plants expressing pharmaceuticals or other substances **that are not related to food**.*

We propose to replace the word "*alter*" with "*modified*" on item b. This change will be consistent with the terminology through the title of the draft, other sections and previous documents. Besides, the word "alter" can be interpreted as having a pejorative meaning when translated into Spanish, while the translation of "modified" is neutral.

Besides, we propose to replace the term "not related to food" with "not intended to be present in food". We cannot anticipate (especially regarding health benefits) if a substance that is not usually present in foods may be introduced safely to incorporate nutritional or health benefits.

**• Impact of post-harvest factors**

**Section 2 – Assessment Strategy**
**- Characterization of the change introduced**

Stability of the level of expression and Impact of post-harvest factors on stability *Many aspects related to stability are already covered in the Plant Guideline. However, it is suggested that additional aspects of stability specifically related to rDNA plants modified for nutritional or health benefits be clearly noted and elaborated in the Annex, as appropriate. Particular attention should be given to the impact of various growing conditions encountered in developing countries on the expression of the particular trait in staple crops. The impact of* ***post-harvest factors such*** *as customary conditions of packaging, storage, distribution, and use on the stability of the nutrient or related substance should be considered as part of the assessment.*

For clarification purposes, we propose to insert the term "on food safety risks" in the last sentence, so it would read "The impact of post-harvest factors *on food safety risks*, such as customary…"

**• Staple Crops - Developing Countries**

**Section 2 – Assessment Strategy**
- **Characterization of the change introduced**

*[…]Particular attention should be given to the impact of various growing conditions encountered in developing countries on the expression of the particular trait in staple crops.*

*[…] A particular emphasis should be placed on the impact of bioavailability of nutrient in staple crops of interest to populations in developing countries.*

The diversity of growing conditions is more related to the geographical extension and location of countries, and not so much to their socioeconomic development. So it may be true that the impact of various growing conditions available throughout the globe is important, but in any case this consideration is applicable to foods originated in developed as well as developing countries. Furthermore, it will be applicable to staple and not-staple crops. In fact, the cultivation of some non-staple crops is quite restricted to certain regions, and there is little information on the cultivation in other areas, so this issue may be even more important for non-staple crops.

We recognize that staple crops imply food supply dependence, and a large level of exposure both in terms of people exposed and quantity of food ingested. Nevertheless, staple crops are not exclusive of developing countries. Moreover, some developed countries seem to be facing food-related problems (e.g. obesity, high cholesterol levels) related to socio-cultural issues and despite of the abundance of "healthy" food options.

We do appreciate the good will and concerns of some delegations regarding the interests of developing countries. But actually we do not identify any scientifically-based reason in this area to sustain different criteria for separate countries/regions. Neither have we identified any scientifically-based sound argument to apply specific considerations for staple crops compared to other crops. And we think that the introduction of unnecessary differentiations is against the mission of the Codex Commission, so we propose not to include in this document any reference to staple crops or developing countries.

Nevertheless, if other delegations can identify relevant guidance regarding staple crops based on their larger dietary contribution, Argentina proposes to replace the word "developing" with "different" in the first sentence quoted, and to delete "of interest to populations in developing countries" in the second one.

**• Definition of "Nutrient"**

**Appendix 2: Terms and Definitions**

*Terms and definitions which may be relevant to this work are outlined below with appropriate references:*

*Nutrient and related substances - (excerpt from the Report of a Joint FAO/WHO Technical Workshop on Nutrient Risk Assessment, 2- 6 May 2005) not specifically defined for this report, but regarded as inherent constituents of food that are either biologically essential or have a demonstrated favourable impact on health. They do not encompass food additives or substances such as food contaminants, pesticides, microbiological pathogens, or other foodborne hazards. National/regional regulatory authorities vary in their definitions for nutrient substances; however, scientific evidence to assess risk from such substances should in principle be equally relevant for all countries.*

*Nutrient - (excerpt from General Principles for the addition of essential Nutrients to Foods -CAC/GL 09-1987 (amended 1989, 1991) means any substance normally consumed as a constituent of food:*
*(a) which provides energy; or*
*(b) which is needed for growth and development and maintenance of healthy life; or*
*(c) a deficit of which will cause characteristic biochemical or physiological changes to occur.*

We find advantages and disadvantages in both definitions, so we suggest the working group should consider discussing a specific definition for this guideline, which would be more appropriate for the present goal.

**• Definition of "Conventional Counterpart"**

We note the definition of "Conventional Counterpart" of the main text of the plant guideline:

*"a related plant variety, its components and/or products for which there is experience of establishing safety based on common use as food"*

and the further guidance of art 51:

*"When the modification results in a food product, such as vegetable oil, with a composition that is significantly different from its conventional counterpart, it may be appropriate to use additional conventional foods or food components (i.e. foods or food components whose nutritional composition is closer to that of the food derived from recombinant-DNA plant) as appropriate comparators to assess the nutritional impact of the food"*

We suggest considering the range of potential appropriate comparators for foods derived from nutritionally enhanced plants, in order to determine if current guidance is sufficient to enclose every possible comparator that would be useful to comprise.

**AUSTRALIA**

Australia would like to express its appreciation to the Government of Canada for leading the electronic Working Group, and for producing the abovementioned scoping document for discussion at the 6th session of the Task Force in Chiba, Japan.

Australia provided detailed comments to Canada during the development of the scoping document and has no further comments to add at this time, other than to state that we are supportive of the direction being taken in the scoping document and look forward to further discussion of this project at the 6th Session of the Task Force.

**COSTA RICA**

Costa Rica wishes to thank the Government of Japan for its continuing commitment in chairing the Codex Ad Hoc Intergovernmental Task Force on Foods Derived from Biotechnology (TFBT) and for the opportunity to comment on the document:

- **Proposed Draft Annex (Scoping Document) 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.**

Costa Rica considers that this proposed draft annex will be very useful in the future in helping countries apply measures to assess the safety of foods derived from biotechnology.

More specifically, under the Scope of the Annex, in paragraph 10.b, we wish to stress that in the recommendation made by the Electronic Working Group, the phrase "*or their interactions with other components of the plant*" could be misinterpreted, causing delays in decision-making, if greater importance were to be given to assessing other possible minor compounds that were not the purpose of the intended modification. Costa Rica requests that this phrase be tabled for discussion by the Task Force.

**EUROPEAN COMMUNITY**

The European Community and its 25 Member States (ECMS) wish to thank Canada for the successful lead of the electronic working group developing a guideline for the Conduct of Food Safety Assessment of Foods derived from recombinant-DNA Plants modified for Nutritional or Health benefit in the form of an annex to CAC/GL 44-2003.

The ECMS wish to make the following comments to the report of the electronic working group:

***Selection of the most appropriate comparator***

- No mention is made of the comparator to be used along the GM plant for the comparative assessment, including bioavailability studies, which is of particular relevance because the GM plant is supposed to have been changed substantially.
- If the composition of a nutritionally improved GM plant is modified extensively, it may not appropriate to use the near isogenic parental line as the comparator. If no suitable comparator can be identified within the same crop or if no appropriate comparator is available, e.g. for field trials, the safety assessment may not concentrate on identified differences to a traditional crop with a history of safe use and a full safety assessment focusing on the levels of the food constituents in the context of the proposed use and intake of the food may be necessary.

- It may be considered to include the non-modified plant with and without external fortification as comparators (NB point 20 recognizes that biofortification may be different from conventional fortification). In addition, additional comparators may comprise other plants with similar composition to the genetically modified one, such as has been done in literature with vegetable oils with altered composition (e.g. GM canola oil that is high in gamma linolenic acid has been compared to borage oil). Certain intricacies need being considered such as the form in which the target nutrient occurs in the comparator (e.g. the positions of fatty acid residues in triglyceride molecules may be different), as well as the presence of secondary compounds (e.g. flavonoids, vitamins) with additional health effects.
- The probability of the occurrence of unintended effects in second generation GM plants (for instance plants that have been nutritionally improved by introducing genes to alter/implement metabolic pathways) may be higher compared to the first generation of GM plants. Reference should be given to advanced analytical techniques, e.g. profiling methods, which offer the performance to analyse a broad spectrum food constituents following a non-targeted approach. Although these methods are not currently appropriate for use in safety assessment of either agronomically improved or nutritionally improved crops, the development of these methodologies is progressing very fast.

***a) Estimation of potential exposure/distribution patterns***

- Besides vulnerable groups, also inter-individual variation may be important to consider (point 15). In particularly, if "worst case" scenarios indicate potential hazards, fine-tuning the exposure estimates with more realistic models, including probabilistic modelling, may become imperative. In addition, besides poor and vulnerable groups, affluent consumers may be the target of health foods in other markets.
- It is recommended mentioning substitution of a particular food item by the improved crop, so that traditional food consumption patterns may not always apply to the new product (point 16). In addition, the omission of the replaced product also has a dietary impact per se.
- It is not clear whether points 15-18 pertain to pre-market exposure assessment only. Post-market monitoring may be needed to verify pre-market assumptions about intake levels of a new food.

***c) Upper limits of safe intake***

- As already expressed in our previous comments, the ECMS acknowledge that the expertise to provide further guidance in this area goes beyond that of the Task Force and welcome the reference to guidance elaborated by other international organizations. However, we are of the view that for nutrient and related substances for which upper limits of safe intake have not been defined, the annex to the Plant Guideline to be developed should recommend to the risk assessor to refer to toxicological studies. Further detail about these studies could be developed under f) and g).

***d) Stability and impact of food processing***

- The scoping document already mentions that additional aspects of stability specifically related to rDNA plants modified for nutritional or health benefits should be clearly elaborated. The importance to consider the impact of food processing not only on the newly introduced trait but also on the composition of the GM products should also be stressed. It is well established that food constituents interact with each other in the course of food processing (e.g. iron – vitamin C – vitamin E) and this should be adequately addressed within the safety assessment where appropriate.

***e) Risk benefit considerations***

- As already expressed in our previous comments, we are of the view that the overall principle should be that the food should not with respect to any properties be nutritionally disadvantageous to the consumer compared to the existing foods that it is intended to replace.
- Possible exceptions are if the newly developed variety has large advantages for one group of consumers, but potential health risks for others that might also need to be assessed at the local level. In such a case, it should be feasible that the final product is consumed by the target consumer group only.
- The ECMS agree with the recommendation of the Working Group that the annex to the plant guideline should give high level guidance regarding the identification and characterisation of the risks and benefits of the modified plant. Benefit and risk are to be expressed in a way they can be weighed up.

***f) Animal feeding studies***

- The scoping document refers to the Codex Plant Guideline, of which point 53 mentions animal feeding studies in a concise way (point 36). Animal feeding trials for safety and nutritional testing of GM plants modified for nutritional or health benefits should be more elaborated. In addition, it may be useful to have some thoughts on the appropriateness of animal models for testing human foods (e.g. animal models for beta carotene uptake and metabolism may still show differences between species and between humans and animals).

**JAPAN**

Japan would like to thank the Canadian Government who led the electronic Working Group and other WG members for its excellent work in elaborating the scoping document of an Annex to the "Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plant Modified for Nutritional or Health Benefits". Japan generally supports the approach which this scoping document takes, and would like to provide general comments to go further with this project. As described in the Report of the e-WG, many aspects raised in this draft scoping document are already covered in the existing Plant Guideline or are not unique to the recombinant-DNA plants modified for nutritional or health benefits. Therefore, it may be practical and useful that this Annex limits its scope to the safety and nutritional issues which are specific to foods derived from recombinant-DNA plants modified for nutritional and health benefits, and provides a greater focus on staple crops of interest to populations in developing countries along with the Project Document (see "3. The main aspects to be covered" of the Project Document, APPENDIX III, ALINORM 06/29/34).

Specific Comment for Draft Annex

- **Section 1 – Introduction**

To define the scope of this Annex more precisely, we would like to propose to revise the last sentence of the "Scope" as follows:

*"The Annex does not cover plants ~~expressing~~* ***modified for*** *pharmaceuticals~~s~~ or other ~~substances that are not related to~~* ***non-****food* ***use****."*

**KENYA**

We recognize that all inputs made by countries participating in the working group led by Canada were considered in drawing up the recommendations and the scope of the annex. Therefore, we support the recommendations made by the working group and the subsequent outline. We also wish to recognize the following:

**Section 2- Assessment Strategy**

**Characterization of the Change Introduced**

1) Stability of the level of expression and impact of post harvest factors.

Some of the conditions likely to affect expression of traits and nutrient stability include use and non-use of fertilizers and pesticides, and post-harvest exposure to uncontrolled environmental elements for example temperatures and humidity in traditional storage and distribution system, and open-air markets found in developing countries.

2) Bioavailability

We recognize that some crops, for example sorghums and legumes have natural factors that inhibit availability of essential minerals, while white fleshed sweet potatoes have low level of vitamin A. It is appropriate that assessment is made to ensure that r-DNA plants modified for nutritional and health benefits significantly improve the bio-availability of the nutrients in such foods without having negative health effects on the target populations. And in addition, the modification of such foods should not enhance bioavailability of other substances that require limited exposure like nitrates.

**Estimation of Potential Exposure /Distribution Patterns**

Exposure Assessment

We recognize that other than FAO and WHO documents, individual countries may require to provide national food consumption data to facilitate accurate assessment of nutrient exposure. However, developing countries such as Kenya may not have national food consumption data that could be useful in supporting internationally identified upper limits for safe intake.

**MEXICO**

**Draft Annex: Food Safety Assessment of Foods Derived from Recombinant-DNA Plants Modified for Nutritional or Health Benefits**

In our opinion, the document still lacks the maturity to provide the consistency and substance needed for analysis as a draft annex to the Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants (CAC/GL 45-2003). It would be better to wait until the annex contains technical specifications to guide the conduct and complementarity of risk assessment.

We note the repeated differentiation in assessment for developing countries and staple crops.

We see no scientific justification for this discrimination.

We consider the terms "nutritional benefits" and "health benefits" should be defined in accordance with the determinations of the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU).

**Section I – Introduction**
**Scope**

The scope is defined in a complete and precise manner.

**Section II – Assessment strategy**
**Characterization of the change introduced**

Aspects relating to the stability of genetic modification are already covered in the Plant Guideline, regardless of the modification introduced, and do not therefore need to be revisited in this annex.

We consider it discriminatory and scientifically unjustified to associate assessment of the impact of modification with the growing conditions of developing countries. This aspect is unrelated to GMO or staple crop status and relates to adjustment to the agronomic and climatic conditions of individual countries. We propose removing this from the draft annex.

Although the impact of post-harvest factors on the introduced trait is already covered in the Plant Guideline, we consider it appropriate to consider this aspect in the risk assessment of this particular type of genetically modified plant. The risk assessment should examine whether the product expressed in the recombinant DNA plant is bioavailable and check that its composition, concentration and bioavailability in estimated intake is not significantly altered in post-harvest operations, storage, distribution, processing and culinary use.

**Bioavailability**

There is currently no valid method for testing bioavailability, which needs to be developed with the Codex Committee on Methods of Analysis and Sampling (CCMAS). What is essential is to determine that the trait expressed in the food derived from biotechnology is bioavailable to consumers in such a way that consumption of the food in similar quantities to its conventional counterpart, under the normal practices and customs of each country, will provide sufficient quantity of the compound that generates the health or nutritional benefit.

The paragraph on bioavailability is vague and ambiguous, as it fails to clarify "aspects of bioavailability specifically related to rDNA plants modified…" or "other aspects of bioavailability [that] may be general in nature". We suggest these two points be clarified.

**Estimation of potential exposure/distribution patterns**
**Exposure assessment**

As with bioavailability, the text is ambiguous and vague when it states "any aspects are identified as specifically relating to rDNA plants modified for nutritional or health benefits".

Risk assessment should consider consumption aspects, as the introduction of foods derived from biotechnology with nutritional or health benefits could encourage people to consume other than traditional levels of a specific type of food to achieve certain benefits. Normal consumption levels and patterns could therefore change, with a subsequent impact on nutritional status from possible changes in profile of macro- and micronutrient intake, with consequent effects on consumer health.

Exposure assessments conducted under risk assessments before a product is marketed may not cover circumstantial exposure scenarios. Hence the need for more focused estimation of exposure or estimation of consumption among specific risk groups. Post-market monitoring, as a risk management measure, could be conducted in such cases and in follow-up to a **scientifically based hypothesis of risk to health** to provide additional information that would validate or refine exposure scenarios, especially for vulnerable populations.

When the hypothesis applies to recombinant DNA plants that express a particular nutritional trait aimed at specific population groups, exposure assessment should only target those groups.

**Assessment of potential nutritional and health outcomes**
**Upper limits of safe intake**

We suggest this item be removed as it fails to provide any precise guideline on how to assess this aspect. Besides, the risk aspects are analysed in the paragraph on risk/benefit considerations.

**Identification and characterization of risks and benefits**

This item should consider aspects relating to level of risk and verification of the benefits claimed for the GM food.

It would be best to begin by determining whether the compound expressed by the recombinant DNA plant really does generate a health benefit. Relevant are the documents under examination by the Codex Committee on Nutrition and Foods for Special Dietary Uses.

We should then examine whether consumption of the recombinant DNA plant would be sufficient in quantity and bioavailability to produce the desired effect, considering patterns of use and consumption of this food by the target population, cultural diversity, vulnerable subgroups and other factors.

Post-market monitoring may be required to confirm the assumptions of **a scientifically based risk hypothesis** and to verify the health effects of foods derived from recombinant DNA plants modified for nutritional or health benefits.

**NEW ZEALAND**

New Zealand is pleased to submit the following comments on the *Proposed Draft Annex (scoping document) 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.*

New Zealand supports the general approach taken by the electronic working group, led by Canada, and the framework of the draft annex. New Zealand looks forward to contributing to the further development of this annex.

New Zealand notes that the science in the area of nutrition is dynamic and evolving and as such guidance provided through the draft text should be at a relatively high level. It should not prescribe an exclusive list of the factors that may need to be considered when conducting a safety assessment of foods derived from rDNA plants modified for nutritional or health benefits.

New Zealand also notes the work being done in CCNFSDU on nutritional risk assessment, and believes that it is important to align the work being undertaken in this a Task Force with that of CCNFSDU.

New Zealand has some specific comments to make with regard to the scope of the draft annex.

New Zealand considers that the use of the word "anti- nutrient" in the scope of the proposed draft annex is not useful as a number of nutrients can behave in an "anti-nutrient" manner in some environments. For example, interactions between zinc and calcium – zinc will inhibit the absorption of calcium in some circumstances and yet is also a nutrient. Accordingly, New Zealand suggests replacing the word "anti-nutrient" in the scope of the annex with "positive and/or negative interactions". By leaving the wording broad there is the potential to pick up both positive and negative nutritional aspects that may not be covered in the original wording.

New Zealand also notes that the scope of the proposed draft annex currently refers to toxins and allergens. New Zealand considers that toxins and allergens are already adequately addressed within the plant guidelines. Therefore, additional guidance is not required in this annex.

New Zealand suggests the following alternative wording within the scope of the draft annex:

(b) *the particular trait aims to alter the nutritional value of the product and impacts on aspects such as the presence, quantity or bioavailability of a nutrient or related substance, or their positive and/or negative interactions with other components of the plant, to achieve an intended nutritional or health benefit.*

**UNITED STATES OF AMERICA**

The United States welcomes this opportunity to comment on the Agenda paper CX/FBT 06/6/5 — Proposed Draft Annex (Scoping Document) 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*. The U.S. would like to express its appreciation to the Government of Canada for leading the electronic Working Group and for producing the scoping document for discussion at the 6th session of the Task Force. The U.S. believes that this document provides an excellent starting point for discussions on the project *Annex: Recombinant-DNA Plants Modified for Nutritional or Health Benefits*.

The United States provided detailed comments to the electronic Working Group during the development of the scoping document and has no additional technical comments at this time. The U.S. is supportive of the direction taken in the scoping document and looks forward to further discussion of this project at the 6th Session of the Task Force.