codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

JOINT OFFICE: Viale delle Terme di Caracalla 00100 ROME Tel: 39 06 57051 www.codexalimentarius.net Email: codex@fao.org Facsimile: 39 06 5705 4593

**Agenda Item 5**

**CX/FBT 06/6/5**
**August 2006**

**JOINT FAO/WHO FOOD STANDARDS PROGRAMME**

**E**

**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

Governments and international organizations wishing to submit comments on the following subject matters are invited to do so **no later than 1 October 2006,** preferably in electronic format, for the attention of Dr. FUJII Mitsuru, Fax No.: +81 3 3503 7965; E-mail: codexj@mhlw.go.jp with a copy to the Secretary, Codex Alimentarius Commission, Joint FAO/WHO Food Standards Programme, Viale delle Terme di Caracalla, 00100 Rome, Italy (Fax +39.06.5705.4593; E-mail: Codex@fao.org).

1. The Fifth Session of the Codex *Ad Hoc* Intergovernmental Task Force on Foods Derived from Biotechnology agreed to start new work to elaborate a 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 (ALINORM 06/29/34, para.37).

2. The new work proposal was approved by the 29th Session of the Codex Alimentarius Commission as N02-2006 (ALINORM 06/29/41, Appendix VIII).

3. The Sixth Session of the Task Force is invited to discuss 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 as presented in Appendices 1 and 2 of the attached Report of the Working Group led by Canada.

**Report of the Electronic Working Group on the Proposed Draft Annex to the Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants: Food Safety Assessment of Food Derived from Recombinant-DNA Plants Modified for Nutritional or Health Benefits**

## Background

1. At its fifth session, the Codex *Ad Hoc* Intergovernmental Task Force on Foods Derived from Biotechnology agreed to initiate new work in the form of an Annex to the Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants (CAC/GL 45-2003), hereafter referred simply as the Plant Guideline, and proceed with further scoping of the work on the basis of the Project Document.

2. The Task Force agreed to establish an electronic working group led by Canada to formulate a proposed draft document (scoping document) to be presented at the next session of the Task Force. Interest in participating in the Electronic Working Group was expressed by 37 member countries, 1 member organization and 6 observers[1].

3. Circular letter CL 2005/46-FBT was distributed in October 2005 to solicit comments on this work. Concurrently, Canada sent a complementary letter to all Codex members to confirm members of the electronic working group and to assist in the preparation of their responses to CL 2005/46-FBT by providing a questionnaire.

4. The invitation for comments was accepted by 20 member countries, 1 member organization and 2 observers. Canada reviewed the responses and developed a *Working Document* for further consideration by the Electronic Working Group. The *Working Document* outlined suggestions regarding the scope of the Annex and specific elements for inclusion.

5. The *Working Document* was circulated to the Electronic Working Group in April 2006 for consideration and input. The invitation for comments was accepted by 11 member countries. This *Report from the Electronic Working Group* is the result of both consultations.

## Draft Scoping Document

6. The objectives of this document are to determine the recombinant-DNA (rDNA) plants to be within the compass of the Annex to the Plant Guideline and the related elements of food safety and nutritional assessment to be considered for inclusion. These two components are elaborated in this document, along with specific recommendations from the Electronic Working Group.

7. A proposed draft outline of the Annex: Food Safety Assessment of Food Derived from Recombinant-DNA Plants Modified for Nutritional or Health Benefits is included in Appendix 1. Some relevant terms and definitions which have been taken into account for the elaboration of this document are included in Appendix 2.

## Scope of the Annex

8. Based on the Project Document (Appendix III of ALINORM 06/29/34), the Annex should provide further guidance to the Plant Guideline with respect to any additional safety and nutritional considerations related to the assessment of foods derived from nutritionally enhanced rDNA plants. The scope of this work should not cover plants expressing pharmaceuticals or other non-food related substances as the purpose of these plants is not for

[1] Argentina, Australia, Austria, Belgium, Brazil, China, Costa Rica, Cuba, Denmark, European Community, Egypt, Finland, France, Germany, Indonesia, Italy, Iran, Kenya, Japan, Madagascar, Mexico, Mongolia, the Netherlands, Nepal, New Zealand, Norway, Pakistan, the Philippines, Republic of Korea, South Africa, Switzerland, Spain, Sweden, Thailand, Turkey, Uganda, the United Kingdom, the United States of America, Biotechnology Industry Organization, Consumers International, CropLife International, Enzyme Technical Association, International Council of Grocery Manufactures Associations and the European Association for Bioindustry.

food use but rather for use as factories to produce industrial or pharmaceutical compounds.

9. Issues that are common to both rDNA plants and foods in general should be carefully considered to ensure they fall under the mandate of the Task Force so to ensure the Task Force is not duplicating the work of other Codex committees such as the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU).

*Recommendation from the Electronic Working Group:*

10. *Based on input received by members of the Electronic Working Group a draft scope is being proposed. The text represents a combination of members' suggestions into the following paragraphs as follows:*

*"The following factors determine whether an rDNA plant is an ArDNA 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."*

**Elements Considered for Inclusion**

11. As outlined in Section 2 of the Project Document (Appendix III of ALINORM 06/29/34), the Plant Guideline describes the recommended approach to carry out safety assessment of food derived from rDNA plants. It also provides general guidance with respect to intentional nutritional modification (paragraphs 48-53 of the Plant Guideline). In particular, it is stated that *foods derived from rDNA plants that have undergone modification to intentionally alter nutritional quality or functionality should be subjected to additional nutritional assessment - beyond that conducted when modifications are for other purposes - to assess the consequences of the changes and whether the nutrient intakes are likely to be altered by the introduction of such foods into the food supply*.

12. As outlined in Section 3 of the Project Document, additional safety and nutritional considerations for the assessment of foods derived from rDNA plants modified for nutritional or health benefits include such aspects as bioavailability and physiological function of the intended modification. Particular focus will be given to staple crops of interest to populations in developing countries.

13. The Plant Guideline already addresses to some degree: exposure assessment and bioavailability/stability (paragraph 49); change of nutrient profile through intended and unintended modification (paragraph 50); consideration of particular populations with different geographical and cultural conditions (paragraph 52); and additional testing including animal feeding (paragraph 53). The Annex is only to include guidance that is supplemental to the Plant Guideline.

14. The Electronic Working Group elaborated on the elements to be included in the Annex and provided specific recommendations for consideration by the Task Force. It was also recommended that the document *A Model for Establishing Upper Levels of Intake for Nutrients and Related Substances. Report of a Joint FAO/WHO Technical Workshop on Nutrient Risk Assessment. WHO Headquarters, Geneva, Switzerland, 2-6 May 2005* be taken into consideration during the elaboration of the Annex as it is pertinent to many of the elements recommended for inclusion.

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

15. This parameter was found useful by most Working Group members to identify potential benefits and adverse effects for target groups and other segments of a population. The limited access to a wide variety of food products in developing countries is also an important factor to consider particularly among poor and vulnerable groups. Such analysis is important for establishing upper limits of safe intake, identify potential interactions with other components of the diet and determine whether certain labels are required to better target a sub-population.

16. Important elements to consider are: the properties of the new or enhanced nutrient or related substance; the vulnerable groups in relation to the modified trait; the health status of a given population; consumption patterns including the significance of the crop species, including staple crops, as a component of the diet; and, in the specific case of rDNA plants, whether the plant is likely to be consumed raw or as an ingredient of a processed food.

*Recommendation from the Electronic Working Group:*

17. *Exposure estimation is recognized as an important element to consider. However, most, if not all, aspects of exposure estimation are not unique to rDNA plants enhanced for nutritional or health benefits. It is recommended that if any aspects are identified as specifically relating to rDNA plants modified for nutritional or health benefits, that they be clearly noted and elaborated in the Annex.*

18. *In addition, aspects of exposure estimation that are general in nature may be covered in the Annex through high-level guidance and with reference to appropriate documents. The document A Model for Establishing Upper Levels of Intake for Nutrients and Related Substances. Report of a Joint FAO/WHO Technical Workshop on Nutrient Risk Assessment. WHO Headquarters, Geneva, Switzerland, 2-6 May 2005 is particularly relevant to this topic. Reference to any relevant modelling of potential intakes resulting from vitamin and mineral addition to foods would also be useful including FAO Regional Diets Data.*

***b) Bioavailability***

19. Bioavailability varies considerably between individuals based on their diet, age and health status. Furthermore, the functional roles of related compounds (other than well known nutrients) are often not clearly established as exerting a health benefit. It was noted by Working Group members that bioavailability assessment may be necessary particularly when the modification intends to change the level of an existing, or to produce a new, nutrient or related substance in a particular crop species. In some cases, it may be necessary to demonstrate that there is no unintended change in bioavailability of other nutrients and anti-nutrients, or to determine unintended effects such as interaction with other components of a diet.

20. There may be factors specific to rDNA plants modified to alter levels of nutrients compared to foods that have been conventionally fortified. For example, more than one chemical form of a nutrient may be expressed as a result of a modification and these various forms may not be equivalent in their bioavailability. Concentration levels of the nutrient or related substance may also impact on bioavailability. This contrasts with a conventional fortification scenario where typically a single, stable chemical form of a nutrient is added to the food at a controlled concentration during manufacture and processing.

21. While it was noted that no ideal testing method of bioavailability is yet available and the results obtained will be dependent upon the method applied, a reference[2] for assessing bioavailability has been presented.

[2] "Biodisponibilité – Guide pour l'étude de la biodisponibilité des nutriments alimentaires". July 2004. Coordinator: Hélène Marfaing, CEVA. – Text provided in French.

*Recommendation from the Electronic Working Group:*

22. *It is recommended that aspects of bioavailability specifically related to rDNA plants modified for nutritional or health benefits (as per noted in paragraph 20) be clearly noted and elaborated in the Annex. A particular emphasis should be placed on the impact of bioavailability of nutrient in staple crops of interest to populations in developing countries.*

23. *Other aspects of bioavailability may be general in nature and go beyond foods derived from rDNA plants. We recommend that these latter aspects be covered in the Annex only through high-level guidance and by providing pertinent information through appropriate references.*

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

24. Working Group members recognized that safe upper intake levels should be determined for nutrients and related substances to prevent excessive intake by vulnerable populations. It was also recognized that there is a need to determine the safety of nutrients and related substances when upper limits have not been determined and to also consider the history of safe use of the nutrient when appropriate. However, it was also recognized that the issue was generic in nature, not unique to rDNA plants, and that necessary guidance would be best provided by CCNFSDU.

25. Many Working Group members indicated that significant amount of work has already been done in this area. For example, the Institute of Medicine has determined upper limits for a number of nutrients and the European Food Safety Authority (EFSA) has similar work on this subject[3].

*Recommendation from the Electronic Working Group:*

26. *Working Group members consider this element important. It is recognized however that the expertise to provide further guidance in this area goes beyond that of the Task Force.*

27. *It is recommended that the Annex include text to the effect that the food safety assessment should verify that Upper Limits of Safe Intake for nutrients and related substances are being considered and that guidance from Codex Alimentarius (through CCNFSDU) is being followed. Information provided by relevant WHO references (Vitamin and Mineral Requirements in Human Nutrition, Second Edition, WHO, 2004; A Model for Establishing Upper Levels of Intake for Nutrients and Related Substances. Report of a Joint FAO/WHO Technical Workshop on Nutrient Risk Assessment. WHO Headquarters, Geneva, Switzerland, 2-6 May 2005 may be used when such guidance is not provided by the Codex Alimentarius.*

*d) **Stability***

28. Working Group members were of the view that stability aspects were important, however, many generic aspects were already appropriately covered in the Plant Guideline.

29. An important consideration specific to rDNA plants was noted regarding the level of expression of the trait that may vary under different environments (i.e., growing conditions, climates, stress factors, maturity of the plant at harvest, use of pesticides, etc.). The variability in the level of expression should be well established as this would have an impact on the evaluation of the human exposure. Particular attention should be given to the impact of these factors on the expression of particular traits in staple crops and the implications for populations of developing countries.

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

[3] "Tolerable Upper Intake Levels for Vitamins and Minerals". February 2006. EFSA.

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.

*Recommendation from the Electronic Working Group:*

31. *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.*

***e) Risk/benefit consideration***

32. Some Working Group members expressed the view that there should be a distinction between the food safety assessment as elaborated in the Plant Guideline and the nutritional assessment covered in paragraphs 48 to 53 of the Plant Guideline, which may be further elaborated in the Annex. It was noted that the risks identified in the food safety assessment should not be outweighed by benefits identified in the nutritional safety assessment so that foods modified for nutritional or health benefits do not end up with lower safety standards than rDNA plants modified for other purposes. It was further suggested by some Working Group members that the benefit of the modified plant should be a pre-requisite (i.e., that it should materially improve health) to ensure that the rDNA plant modified for a nutritional or health benefit is pertinent.

33. Some Working Group members were of the view that risks and benefits should be identified and characterized but that the consideration of weighing up the risks versus the benefits was more relevant to risk management and therefore not within the scope of the Annex.

*Recommendation from the Electronic Working Group:*

34. *It is suggested that high level guidance regarding the identification and characterization of the risks and benefits be elaborated in the Annex but that guidance on how to weigh the risks versus the benefits not be included.*

***f) Animal feeding studies***

35. Some Working Group members were of the view that the use of animals to evaluate safety aspects was already appropriately covered in the Plant Guideline. Within the context of the Annex, the purpose of such studies would be for assessing nutritional impacts rather than food safety. Some Working Group members were of the view that animals were unlikely to make good models for studying human nutritional implications and that the types of studies that may be most useful would depend on the particular issue to be addressed. Furthermore, considerations regarding the use of animal models to determine Upper Limits of Safe Intake are not unique to rDNA plants modified for nutritional or health benefits and therefore should not be within the scope of the Annex.

*Recommendation from the Electronic Working Group:*

36. *Based on input from the Working Group this element does not appear to warrant further guidance in the Annex beyond that provided in the Plant Guideline. It is suggested, therefore, that the Annex do not elaborate on this element.*

***g) Study Design***

37. Study design encompasses all aspects of the safety assessment to ascertain that the rDNA plants express the trait in the way it was intended. The effect of processing, the nutrient level in various parts of the plant and its stability over time and processing should all be part of the study design.

Many Working Group members believed that the Plant Guideline adequately covered this element. Others were of the view that there would be value in further considering the need for additional guidance, however, no specific elements were identified by Working Group members as warranting further elaboration in the Annex.

*Recommendation from the Electronic Working Group:*

38. *There were no additional aspects identified which may warrant further guidance beyond that provided in the Plant Guideline. It is therefore recommended that the Annex does not address this element.*

**Appendix 1: Proposed Draft Outline of the Annex with Recommendations from the Electronic Working Group**

**DRAFT ANNEX: FOOD SAFETY ASSESSMENT OF FOOD DERIVED FROM RECOMBINANT-DNA PLANTS MODIFIED FOR NUTRITIONAL OR HEALTH BENEFITS**

**Section 1 – Introduction**

- Scope

*Based on input received by members of the Electronic Working Group a draft scope is being proposed. The text represents a combination of members' suggestions into the following paragraphs as follows:*

> *"The following factors determine whether an rDNA plant is an ArDNA 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;*
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>
> *The Annex does not cover plants expressing pharmaceuticals or other substances that are not related to food."*

**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.*

Bioavailability

*It is recommended that aspects of bioavailability specifically related to rDNA plants modified for nutritional or health benefits (as per noted in paragraph 20) be clearly noted and elaborated in the Annex. A particular emphasis should be placed on the impact of bioavailability of nutrient in staple crops of interest to populations in developing countries.*

*Other aspects of bioavailability may be general in nature and go beyond foods derived from rDNA plants. We recommend that these latter aspects be covered in the Annex only through high-level guidance and by providing pertinent information through appropriate references.*

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- **Estimation of potential exposure/distribution patterns**

Exposure assessment

*Exposure estimation is recognized as an important element to consider. However, most, if not all, aspects of exposure estimation are not unique to rDNA plants enhanced for nutritional or health benefits. It is recommended that if any aspects are identified as specifically relating to rDNA plants modified for nutritional or health benefits, that they be clearly noted and elaborated in the Annex.*

*In addition, aspects of exposure estimation that are general in nature may be covered in the Annex through high-level guidance and with reference to appropriate documents. The document A Model for Establishing Upper Levels of Intake for Nutrients and Related Substances. Report of a Joint FAO/WHO Technical Workshop on Nutrient Risk Assessment. WHO Headquarters, Geneva, Switzerland, 2-6 May 2005 is*

*particularly relevant to this topic. Reference to any relevant modelling of potential intakes resulting from vitamin and mineral addition to foods would also be useful including FAO Regional Diets Data.*

- **Assessment of potential nutritional and health outcomes**

Upper limits of safe intake

*Working Group members consider this element important. It is recognized however that the expertise to provide further guidance in this area goes beyond that of the Task Force.*

*It is recommended that the Annex include text to the effect that the food safety assessment should verify that Upper Limits of Safe Intake for nutrients and related substances are being considered and that guidance from Codex Alimentarius (through CCNFSDU) is being followed. Information provided by relevant WHO references (Vitamin and Mineral Requirements in Human Nutrition, Second Edition, WHO, 2004; A Model for Establishing Upper Levels of Intake for Nutrients and Related Substances. Report of a Joint FAO/WHO Technical Workshop on Nutrient Risk Assessment. WHO Headquarters, Geneva, Switzerland, 2-6 May 2005 may be used when such guidance is not provided by the Codex Alimentarius.*

Identification and characterization of risks and benefits

*It is suggested that high level guidance regarding the identification and characterization of the risks and benefits be elaborated in the Annex but that guidance on how to weigh the risks versus the benefits not be included.*

**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 *A Model for Establishing Upper Levels of Intake for Nutrients and Related Substances. Report of a Joint FAO/WHO Technical Workshop on Nutrient Risk Assessment. WHO Headquarters, Geneva, Switzerland, 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 food-borne 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.