

CODEX ALIMENTARIUS AND GENETICALLY MODIFIED FOODS

1. WHAT IS CODEX ALIMENTARIUS

The Codex Alimentarius has managed to **stay out of the limelight** in spite of a mandate that concerns all of us (food safety), and in spite of the fact that it exists since more than 40 years. It is hardly ever in the news and it receives not much attention nor by experts of international law nor by many NGO's working on food safety, international trade or environment. This hidden nature of the Codex can probably be explained by the difficulty of categorizing it. First of all, it is a hybrid food safety - trade - environment agency. Secondly, it is not an autonomous intergovernmental organization but a **subsidiary body** of the joint FAO/WHO Food Standards Programme. Nevertheless it administers **multilateral negotiations** among its more than **160 member countries** that are as dynamic, complex and far-reaching as any negotiations taking place in intergovernmental organizations. Thirdly, both of its parent organizations are specialized UN agencies, but the Codex is a quite unique body because of its **very complex** and original **organizational set-up**, based on decentralized work and financing system. It has more than 20 permanent committees and a couple of task forces and working groups, which are all hosted and paid for by different countries. Canada for instance hosts the Codex Committee on Food Labeling, France the one on General Principles, Australia the one on Import/Export control, and Japan hosts the *ad hoc* Codex Intergovernmental Task force on Foods Derived from Biotechnology. This set up allows the organization to function with a budget that is remarkably modest in the face of its heavy and complex mandate, but on the other hand makes it difficult and expensive for NGO's and poor countries to follow on a steady base an issue attending all the important meetings.

The Codex Alimentarius Commission(CAC) was established **1963 as the implementing arm of the Joint FAO/WHO Food Standards Programme.**¹ A quick look at its "charter," namely the 186 page Procedural Manual,² will show immediately that we are dealing here with a major and highly complex intergovernmental instrument. It is very complex because its mandate, i.e. the multilateral negotiation of food safety standards is not only very complex from a scientific standpoint but also fraught with political tensions and cultural traditions which are not easily amenable to global harmonization, one of the Codex's tasks.

Codex Alimentarius is actually the most important **international reference point for developments associated with food standards** in the field of food quality and safety. During the past four decades, all important aspects of food pertaining to the "**protection of the health of consumers and ensuring fair practices in the food trade**" (Art. 1 (a) of the codex statutes) have come under the Codex Alimentarius Commissions scrutiny.

The Codex Alimentarius Commission has been supported in its work by the increasing number of consumers and most governments becoming aware of food quality and safety issues and realizing the need to be selective about the foods people eat. It is now universally accepted maxim that people have the right to expect their food to be safe, of good quality and suitable for consumption as well as be transparently labeled to enabling the consumers to take a fully informed choice.

¹ Understanding the Codex Alimentarius, 1999. Rome: FAO and WHO, 35 p. (7). This is the official publication explaining to a wider public the purpose and functioning of the Codex Alimentarius and its Commission.

<http://www.fao.org/docrep/w9114e/w9114e00.htm>

² Procedural Manual of the Codex Alimentarius Commission, 12th edition, 2001. Rome: FAO and WHO, 174 p. <ftp://ftp.fao.org/codex/manual/Manual12ce.pdf>

2. ORGANIZATION OF CODEX

Codex Alimentarius Commission (CAC), the executive body, is responsible for **final adoption** of standards, guidelines or any other codex text and is giving mandates for new work. Ordinary sessions are being held yearly in Rome (at FAO) or (alternating) in Geneva (WHO).

Standards are being developed through 27 subsidiary bodies consisting of regional, commodity and general committees:

9 General Subject Committees (e.g. on "General Principles" (CCGP), on Food Labeling (CCFL), on Pesticide Residues (CCPR) etc.),

13 Commodity Committees (Fats&Oils, Fish&Fishery, Milk Products etc.),

5 Regional Coordinating Committees (Africa, Asia, Europe, Latin America&Caribbean, North America&Pacific)

For especially focused work Task Forces with mandates limited in time are established by the Commission and Working Groups by Committees.

The work on codex texts in **Committees** or **Task Forces** follows always a clearly defined 8 step procedure and decisions are usually achieved **by consensus**. After having reached step 8 a text is forwarded to the CAC for final adoption.

Membership is open to **all UN Member States**. There are currently 168 codex members and 149 International Non-Governmental Organizations (INGOs) with observer status, representing producers, industry and civil society and 58 intergovernmental organizations.

Based on scientific and technological research as well as discussion a big number of food safety standards and guidelines have been established by Codex in a consensus based decision process with **broad participation of governments, international governmental and non-governmental organizations, food industry and research institutes**. The positive aspect of the decision finding process in Codex Committees, Task Forces and Working Groups is that the NGO's have the possibility to intervene directly and actively in the discussion of new text to propose own wordings or to criticize text proposed by governments or industry. E.g. there is text in the Guideline for Foods Derived from Biotechnology which was proposed as such from NGO side during the Task Force debates.

The negative side is, that industry lobbyists are overrepresented, as well as governments from rich countries. Therefore trade interests are too often given more importance than health, environmental or other civil rights aspects. The south and "civil society" NGO's are only represented in a very small number (nevertheless they could achieve significant successes and have always an important impact).

3. THE IMPORTANCE OF CODEX REGARDING NATIONAL LEGISLATION

Basically Codex standards are voluntary only and therefore thought to be a useful floor for national regulations. But becoming 1995 the **reference point for the WTO SPS-Agreement** on the Application of Sanitary and Phytosanitary measures and the TBT-Agreement on Technical Barriers to Trade³ the significance of Codex increased drastically. The SPS language in effect

³ SPS-Agreement, Annex A – Definitions:

«3. *International standards, guidelines and recommendations*

a) for food safety, the standards, guidelines and recommendations established by the Codex Alimentarius Commission relating to food additives, veterinary drug and pesticide residues, contaminants, methods of analysis and sampling, and codes and guidelines of hygienic practice.»

TBT Agreement, Article 1.1 *General Provisions*

«General terms for standardization and procedures for assessment of conformity shall normally have the meaning given to them by definitions adopted within the United Nations system and by international standardizing bodies taking into account their context and in the light of the object and purpose of this Agreement.»

made **Codex standards more like a ceiling**, beyond which scientifically not justifiable requirements were in effect that could be seen as **unjustified barriers to trade** (according to SPS and TBT).

WTO member states could be 'pressured' by a Codex decision into lowering their own standards, not adhering to Codex decisions could create serious legal complications in future WTO disputes. The SPS agreement takes precedence over the TBT Agreements in its domain of application, i.e. in import restrictions of a biological or medical nature. Nevertheless, the TBT Agreement is also important with regards to the Codex, especially with regards to the thorny and unresolved issue of the rights an importing country may have to insist on the **mandatory labeling** of GM products – not to talk from an **import restriction** or complete ban. For the time being, a Codex Guideline which supports mandatory GM food labeling (based on a Commission request from 1991) still being in the process of developing/discussion in the **Codex Committee on Food Labeling** (actually step 3 of 8), a threat of a WTO complaint by GM food exporting countries as USA, Canada or Argentina against governments implementing mandatory labelling for GM foods is more or less banned. But the situation would dramatically change, if Codex would stop further work on GM labeling on the basis that there is no reason for GM labeling.

Another example for the direct link between WTO disputes and Codex is the US/Canada/Argentinian complaint against EU's de facto moratorium on GMO's (filed in 2003). In the ruling of the WTO panelists (2006), Codex is mentioned not less than 192 times...

4. CODEX AND GENETICALLY MODIFIED FOODS

The **issue of biotechnology** was first raised by the Codex Commission in **1989** during its 18th session. 1990 a joint WHO/FAO expert consultation convened, and at its 19th session in 1991 the Commission stated that more work on this issue should be done and particularly requested the Codex Committee on Food Labelling to provide guidance on **how the fact that a food was derived from "modern" biotechnologies could be made known to the consumers**. The Commission endorsed the conclusions and recommendations of the Joint FAO/WHO Consultation, that while consumers would benefit from "modern" food biotechnology, some consumers felt that this technology would pose certain problems. For example, individual consumers might, on ethical or other grounds, not wish to buy foods derived from "modern" biotechnology.

1999 the CAC agreed to undertake new work on GM Foods in the concerned Committees and established an ad hoc **Task Force**, hosted by Japan, to work out **standards for GM Foods from 2000-2003**. 2005-2007 a **2nd Task Force** worked out standards for **Foods derived from GM Animals** (specially fish) and 2 annexes on low level GMO presence and foods from GM plants with nutritional benefits. All standards forwarded to CAC for adoption in July 2008.

Codex bodies working on GM foods:

- Codex ad hoc Task Force on Foods Derived from Modern Biotechnology 1 (2000-2003), GM food standards focusing on plants and microorganisms (hosted by Japan)
- Codex ad hoc Task Force on Foods Derived from Modern Biotechnology 2 (2005-2007), GM food standards focusing on animals (especially fish), (Japan)
- Codex Committee on Food Labeling (CCFL), still working on a standard for (mandatory) GM food labeling (Canada/Malaysia)
- Codex Committee for Import/Export control (CCFICS) work on Traceability (Australia)
- Codex Committee on General Principles (CCGP), work on Traceability, Labeling, Risk Analysis, Code of Ethics (France) finalized a (very flawed) wording on traceability at its 20th session May 2004:

"Traceability/product tracing: The ability to follow the movement of a food through specified stage(s) of production, processing and distribution."

and of lower importance:

- Codex Task Force on Animal Feed (Danmark, 2000-2003), decided to stop further work on GM animal feed labeling
- Codex Committee on Methods and Analysis (CCMAS), work on criteria for methods of analysis for foods derived from biotechnology (Hungary)

between the sessions of the committees and task forces several working groups focused on issues as food labeling, traceability, possible allergenicity etc.

5. ACCORDANCE WITH REGULATIONS OF EU, CHINA, AUSTRALIA AND NEW ZEALAND

Regarding the fact that Codex is used as reference in a possible WTO dispute settlement process it is of importance if the actual national/regional regulations are in the frame of the Codex guidelines. As far as I can overview all the important regulations in Europe, Asia and Oceania the new codex guidelines pose no acute threat to these regulations. That means the codex guidelines would not strengthen the US/Canada/Argentina position in a possible WTO complaint against a GM food importing country having regulations on GMO's in force (arguing that these regulations were unjustified trade barriers).

Nevertheless attention has to be given on the future development of codex guidelines, particularly on GM food labeling which is still under work in the Codex Committee on Food Labeling. If the final standard will not contain labeling for information purposes they could pose a threat to any mandatory labeling regime of GMO's in a country member of the WTO.

5. INTERCONNECTION BETWEEN CODEX ALIMENTARIUS AND DIFFERENT MULTILATERAL AGREEMENTS

Besides the already mentioned SPS and TBT agreements of the WTO there is a multilateral environmental agreement with a strong interconnection with Codex Alimentarius: The UN Biodiversity Convention and its **Cartagena Protocol on Biosafety**, adopted 2000 in Montreal.

The development of GMO's (or LMOs as they are called in the Protocol), together with other human intrusions into the state of nature such as the application of pesticides and fertilizers, has stimulated over the past few years an **increased interest for environment-related concerns regarding food safety**. To the extent that agrochemicals and GM seeds promote the expansion of larger and larger monocultures with less and less germplasm diversity, they are at the center of these questions both from the environmental and from the food safety side.

It is clear that the Codex Alimentarius is not considered to be an environmental agreement since it does address food safety aspects and not regulate a sector of the environment such as forests, deserts or the climate. Nevertheless, the dynamics of those Codex negotiations which are of direct concern for the areas of GMO's can only be understood if they are seen as an integral part of the **wider negotiation framework that is called 'trade and environment,'** and which at the multilateral level deals mostly with the relations between the WTO, the Convention on Biological Diversity (CBD) and its Cartagena Biosafety Protocol (BP) administered by the UN Environment Programme (UNEP).

Codex and the **Biosafety Protocol** are **not addressing exactly the same subject matter**. The Codex deals with the safety of all food products, whether living or not (e.g. chocolate), whereas the BP deals with all Living (genetically) modified Organisms (LMOs) whether edible or not (e.g. cotton). Nevertheless, there is a very important **overlap**, especially in the large and commercially huge area of food crops, such as soy beans, corn, or grains, which may represent a threat to biodiversity when they are used as **seeds**. It should be noted also that in developing countries even grains imported as foodstuff are often used as seeds by farmers, especially in a crisis situation.

This interconnection was underlined in the first session of the Codex Task Force on Biotech Foods (2000). The Task Force noted that the Protocol forms part of the international regulatory framework within which the development, adoption, acceptance and use of Codex standards had to be undertaken. The **objective** and provisions **of the Protocol** would therefore **need to be taken into account** during the development of appropriate texts by the **Codex Task Force**. It further noted that the objective of the Protocol was in accordance with the **precautionary approach** contained in Principle 15 of the Rio Declaration on Environment and Development. In the Protocol this approach is (apart from the preamble) clearly embodied in its language, for example in Art. 10:

“**Lack of scientific certainty** due to insufficient relevant scientific information and knowledge ... shall not prevent that Party (i.e. the LMO importer) from taking a decision, ... in order to **avoid** or minimize such **potential adverse effects**.”⁴

The potential decision a country may take which this text refers to of course is nothing else than the application of sanitary or phytosanitary measures which restrict or ban the importation of LMOs.

In the Codex Task Force the debate whether scientific uncertainty should be handled with a “Precautionary approach” or “Precautionary principle” ended always in a clash over two opposed positions which are often called ‘**sound science**’ versus ‘**precaution**’ but the fact of the matter is that both approaches are based on medical, biological, chemical and very generally scientific procedures and techniques; the difference is simply that the European (and civil society NGO’s) approach takes explicitly into account that science provides no answers or unsatisfactory answers to certain questions, and it attempts to integrate this state of knowledge into the regulatory process. Due to US (and other GM Food exporting countries) resistance it was hard to introduce precautionary language into the Codex. The text on premarket safety assessment, ban of antibiotic resistance marker genes, the guideline on possible allergenicity could be interpreted as such a language, the more as the Codex guideline clearly admits that there were **unexpected unintended effects** due to genetic modification which can never be detected or identified with certainty...

This struggle over the concept of coherence has entered the negotiations over the most recent amendments of the Procedural Manual. It contains an appendix “General Decisions of the Commission” dealing in condensed form with principles concerning **the role of science** in the Codex decision-making process, and it addresses the extent to which **factors other than food safety** may be taken into account. At the 24th Session in Geneva in July 2001 a proposed amendment was submitted to delegates containing among other proposals nine points to be added to this appendix.⁵ The 7th point, in brackets, reads as follows

[albeit not within the mandate of the Codex, certain factors may be taken into account, if recommendations of relevant multilateral intergovernmental organizations exist. Codex standards should avoid having a negative impact on the application of such internationally agreed recommendations].

The text of this proposed amendment could be interpreted in the sense, for instance, that the precautionary articles of the BP should be reflected in future changes to the Codex in order to achieve a better coherence with the BP, and to avoid a negative impact on the implementation of the BP. This point, however, was the only one out of the nine that was deleted due to strong opposition from the US delegation. This opposition was certainly in tune with the intentions of

⁴ Cartagena Protocol on Biosafety, *op. cit.*, Articles 10.6 and 11.8.

⁵ ALINORM 01/10, dated May 2001, “Consideration of Proposed Amendments to the Procedural Manual of the Codex Alimentarius Commission,” 8 p.

ICGMA, one of the major lobby groups of the food industry, who argued among other issues raised:

The specific insistence on the inclusion of "other", non-science factors, or factors unrelated to food safety "not within the mandate of Codex" in the discussion of standards and guidelines setting can only reflect a desire to broaden Codex's criteria in the interest of promoting agendas other than food safety.⁶

The ICGMA is undoubtedly quite correct in its interpretation of this proposed amendment. The intention of the drafters of this paragraph might indeed have been to achieve a common strategy in protecting both biodiversity and food safety through coherent policy measures. Then again - what is wrong with this? In fact one might very well argue that the objectives of biosafety and of food safety are at least as compatible as the objectives of food safety and of trade, which as mentioned are two objectives that the Codex is quite able to accept as compatible. This example is an illustration of the difficulties in introducing seemingly obvious concepts like precaution, and coherence with other multilateral agreements, into the Codex Alimentarius. It may also serve as an indicator of the lopsided balance between trade and food safety interests.

One can find, however, in text adopted by the Codex Commission itself, factors, others than purely related to health risks. In the report of the 19th session of CAC (from 1991) it is stated:

"... 90. The Commission ... noted that ... some consumers felt that this technology would pose certain problems. For example, individual consumers might, **on ethical or other grounds**, not wish to buy foods derived from "modern" biotechnology. The Commission requested the Codex Committee on Food Labelling to provide guidance on how the fact that a food was derived from "modern" biotechnologies could be made known to the consumers."

This text is clearly a request for labeling based on the method of production and not on "sound science based health risks". But the fact that this request of the Codex Commission is still not fulfilled by the CCFL after 17 years, shows the problem codex has in dealing with "other legitimate factors".

Perhaps the most worrisome aspect in the Codex's operations is the general impression that **trade interests are given more importance than food safety concerns**. In the short or medium term it has to be assumed that a major realignment of these priorities is very unlikely given the constraints of realpolitik. Nevertheless, there is no reason why one should not be able to arrive at a better balance between the two conflicting interests. That improved balance would at the very minimum require an equal financial participation of FAO (actually 75%) and WHO (25%), and obviously a strengthened input of WHO including at least equal participation in the secretariat activities. Such a financial balance of course would not *per se* achieve an equilibrium between trade and food safety priorities, but it is certainly a precondition - in fact it would represent a precondition which would be relatively easy to achieve in comparison with the modifications that would be required in the other structural factors outlined above. In view of the entrenched trade-oriented US position in other intergovernmental forums, even where the US participates only as observers, the outlook is unfortunately not very bright for any major modifications in the foreseeable future.

⁶ International Council of Grocery Manufacturers Associations, Washington, DC, comments faxed 06/20/01, annexed to Codex cover sheet LIM-9 dated June 2001.

ANNEX:

CODEX ALIMENTARIUS GUIDELINES ON SAFETY ASSESSMENT OF GE FOODS
(SUMMARY AND COMMENTS FROM GREENPEACE)

March 2003 the Ad Hoc Codex Intergovernmental Task Force on Foods Derived from Biotechnology passed after 3-years-discussion 3 guidelines for the **risk analysis and safety assessment of foods derived from biotechnology**⁷ they were formally adopted by the Codex Alimentarius Commission (CAC) in July 2003:

- General Principles for the Risk Analysis of Foods Derived from Modern Biotechnology
- Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants (including Annex on possible Allergenicity of GM foods)
- Guideline for the Conduct of Food Safety Assessment of Foods Produced Using Recombinant-DNA Microorganisms

These guidelines lay out broad general principles intended to make the analysis and management of risks related to foods derived from biotechnology uniform across Codex's 169 member countries. The guidelines concern food safety and not environmental risks.

Provisions of the guidelines include pre-market safety evaluations and product tracing for recall purposes and post-market monitoring. The guidelines cover the scientific assessment of DNA-modified plants, such as maize, soya or potatoes, and foods and beverages derived from DNA-modified micro-organisms, including cheese, yoghurt and beer.

They include provisions for assessing the product's allergenicity, determining if the product may provoke unexpected allergies in consumers. They also consider unintended effects due to the random insertion of DNA sequences into the plant genome which may cause silencing of existing genes, activation of silent genes, or modifications in the expression of existing genes. «Unintended effects may also result in the formation of new or changed patterns of metabolites.»

Of course these guidelines are a compromise and do not fully satisfy the Greenpeace demands. But at least they do not challenge any stricter national/regional legislation on GM foods as for example the new EU regulation on traceability and labelling.

And even if it's not mentioned literally, the precautionary principle is implicitly embodied in the new guidelines: premarket approval and premarket safety assessment, ban of antibiotic resistance marker genes, ban of the use of known allergenes as transgenes are part of the risk and safety assessment outlined in the Codex documents.

The concept of "Substantial Equivalence" is still present in the documents, but the language is clear that such comparing GM foods to non-modified ones is only to initiate and focus the assessment but not a safety assessment itself.

Therefore the guidelines could even be useful to stimulate governments with no or a very weak regulation on GM foods (as a lot of developing countries (or the USA) to start establishing stricter rules regarding GM foods.

⁷ The report of the 4th task force meeting, as the guideline for the food safety assessment of foods produced using rDNA microorganisms (appendix II of the report) are available on www.codexalimentarius.net/reports.asp (doc ALINORM 03/34A) or directly as: ftp://ftp.fao.org/codex/alinorm03/AI03_34e.pdf. The principles for the risk analysis of foods derived from modern biotechnology, the guideline for the conduct of food safety assessment of foods derived from rDNA plants, as the annex on the assessment of possible allergenicity are available as Appendixes II – IV of the doc ALINORM 03/34 (report of the 3rd taskforce session) on www.codexalimentarius.net/reports.asp or directly as: ftp://ftp.fao.org/codex/alinorm03/AI03_34e.pdf.

GENERAL PRINCIPLES FOR THE RISK ANALYSIS OF GE FOODS

Scope and Definitions (§7-8 of the codex text):

«The purpose of these principles is to provide a framework for undertaking risk analysis on the safety and nutritional aspects of foods derived from modern biotechnology. This document does not address environmental, ethical, moral and socio-economic aspects of the research, development, production and marketing of these foods»⁸

Animal Feed issues are addressed in the Codex Task Force on Animal Feeding (report of the 4th session available as <ftp://ftp.fao.org/codex/alinorm03/AI0338ae.pdf>).

The discussion on labeling on GE animal feed is still ongoing there. A vast majority is in favor of such a labeling as a risk management measure, while United States, Australia, Canada and New Zealand are opposed.

Regarding the footnote: It is of concern that genetically modified foods are not completely excluded to serve as «conventional counterparts» used for the concept of substantial equivalence during the safety assessment.

On the other hand the concept of «**substantial equivalence**» **lost his role as a safety assessment in itself**⁹. Some other important positive elements in the codex description of the risk assessment are the following:

Unintended effects have to be taken into account (§11).

«A **pre-market safety assessment should be undertaken...** and should be of a quality and, as appropriate, of quantity that would withstand scientific peer review.» (§12)

«14. Scientific data for risk assessment are generally obtained from a variety of sources, such as the developer of the product, scientific literature, general technical information, independent scientists, regulatory agencies, international bodies and other interested parties. Data should be assessed using appropriate science-based risk assessment methods.

15. Risk assessment should take into account **all available scientific data** and information derived from different testing procedures, provided that the procedures are scientifically sound and the parameters being measured are comparable.»

These paragraphs 14 and 15 indicate clearly that information from the developer of the product only is not sufficient for an adequate safety assessment.

«18. Risk managers should **take into account the uncertainties** identified in the risk assessment and implement appropriate measures to manage these uncertainties.

19. Risk management measures may include, as appropriate, **food labeling**¹⁰, **conditions for marketing approvals** and post-market monitoring.

20. Post-market monitoring may be an appropriate risk management measure in specific circumstances. ... Post-market monitoring may be undertaken for the purpose of:

A) verifying conclusions about the absence or the possible occurrence, impact and significance of potential consumer health effects; and

⁸ This document does not address animal feed and animals fed such feed except insofar as these animals have been developed by using modern biotechnology.

⁹ Draft Guideline for the Conduct of Food Safety Assessment of Foods derived from rDNA plants, §13: «The concept of substantial equivalence...is not a safety assessment in itself; rather it represents the starting point which is used to structure the safety assessment of a new food...»

¹⁰ Reference is made to the CCFL in relation to the Proposed Recommendations for the Labelling of Foods obtained through certain techniques of genetic modification/genetic engineering at step 3 of the procedures

B) monitoring changes in nutrient intake levels, associated with the introduction of foods likely to significantly alter nutritional status, to determine their human health impact.

*21. Specific tools may be needed to facilitate the implementation and enforcement of risk management measures. These may include appropriate analytical methods; reference materials; and, the **tracing of products**¹¹ for the purpose of facilitating withdrawal from the market when a risk to human health has been identified or to support post-market monitoring in circumstances as indicated in paragraph 20.»*

2.2. GUIDELINE FOR THE CONDUCT OF FOOD SAFETY ASSESSMENT OF FOODS DERIVED FROM RDNA-PLANTS

The most important paragraphs:

« SECTION 1 - SCOPE

1. This Guideline supports the Principles for the Risk Analysis of Foods Derived from Modern Biotechnology. It addresses safety and nutritional aspects of foods consisting of, or derived from, plants that have a history of safe use as sources of food, and that have been modified by modern biotechnology to exhibit new or altered expression of traits.

2. This document does not address animal feed or animals fed with the feed. This document also does not address environmental risks.»

...

«SECTION 3 - INTRODUCTION TO FOOD SAFETY ASSESSMENT

...

*11. Animal studies cannot readily be applied to testing the risks safety assessment of foods derived from food plants, including recombinant-DNA plants. This has been addressed by the development of a multidisciplinary approach for assessing safety which takes into account both intended and **unintended changes** that may occur in the plant or in the foods derived from it, using the concept of substantial equivalence.*

*13. The concept of substantial equivalence is a key step in the safety assessment process. However, **it is not a safety assessment in itself**; rather it represents the **starting point** which is used to structure the safety assessment of a new food relative to its conventional counterpart. This concept is used to identify similarities and differences between the new food and its conventional counterpart¹². It aids in the identification of potential safety and nutritional issues and is considered the most appropriate strategy to date for safety assessment of foods derived from recombinant-DNA plants. The safety assessment carried out in this way does not imply absolute safety of the new product; rather, it focuses on assessing the safety of any identified differences so that the safety of the new product can be considered relative to its conventional counterpart.»*

As mentioned before, the clear definition of substantial equivalence as a starting point of the safety assessment signified a big step forward for the Codex guidelines.

«UNINTENDED EFFECTS

14. In achieving the objective of conferring a specific target trait (intended effect) to a plant by the insertion of defined DNA sequences, additional traits could, in some cases, be acquired or existing traits could be lost or modified (unintended effects). ... Safety assessment should include data and information to reduce the possibility that a food derived from a recombinant-DNA plant would have an unexpected, adverse effect on human health.

¹¹ It is recognised that there are other applications of product tracing. These applications should be consistent with the provisions of the SPS and TBT Agreements.

¹² The concept of substantial equivalence as described in the report of the 2000 joint FAO/WHO expert consultations (Document WHO/SDE/PHE/FOS/00.6, WHO, Geneva 2000)

15. **Unintended effects** can result from the random insertion of DNA sequences into the plant genome which may cause disruption or **silencing** of existing genes, activation of silent genes, or **modifications in the expression** of existing genes. Unintended effects may also result in the formation of new or changed patterns of metabolites. For example, the expression of enzymes at high levels may give rise to secondary biochemical effects or changes in the regulation of metabolic pathways and/or **altered levels of metabolites**.

16. Unintended effects due to genetic modification may be subdivided into two groups: those that are "predictable" and those that are "unexpected". ...

17. The safety assessment of foods derived from recombinant-DNA plants involves methods to identify and detect such unintended effects and procedures to evaluate their biological relevance and potential impact on food safety. A variety of data and information are necessary to assess unintended effects because no individual test can detect all possible unintended effects or identify, with certainty, those relevant to human health. These data and information, when considered in total, provide assurance that the food is unlikely to have an adverse effect on human health. ...»

It is recognized in this section that **unintended and unexpected effects** due to genetic modification **occur in GE food plants** and that **it's impossible to exclude any adverse effect on human health** due to these effects.

«FRAMEWORK OF FOOD SAFETY ASSESSMENT

18. The safety assessment of a food derived from a recombinant-DNA plant follows a stepwise process of addressing relevant factors that include:

- A) Description of the recombinant-DNA plant;
- B) Description of the host plant and its use as food;
- C) Description of the donor organism(s);
- D) Description of the genetic modification(s);
- E) Characterization of the genetic modification(s);
- F) Safety assessment:
 - a) expressed substances (non-nucleic acid substances);
 - b) compositional analyses of key components;
 - c) evaluation of metabolites ;
 - d) food processing;
 - e) nutritional modification; and
- G) Other considerations.

19. In certain cases, the characteristics of the product may necessitate development of additional data and information to address issues that are unique to the product under review.

...

21. The goal of each safety assessment is to provide assurance, in the light of the best available scientific knowledge, that the food does not cause harm when prepared, used and/or eaten according to its intended use. ... In essence, therefore, 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.»

SECTION 4 - GENERAL CONSIDERATIONS

This section includes the DESCRIPTION OF THE RECOMBINANT-DNA PLANT, DESCRIPTION OF THE HOST PLANT AND ITS USE AS FOOD, DESCRIPTION OF THE DONOR ORGANISM(S) and, further on:

DESCRIPTION OF THE GENETIC MODIFICATION(S)

«27. **Sufficient information should be provided** on the genetic modification to allow for the identification of **all genetic material potentially delivered to the host plant** and to provide the necessary information for the analysis of the data supporting the characterization of the DNA inserted in the plant.

28. The description of the transformation process should include:

A) information on the specific method used for the transformation (e.g. *Agrobacterium*-mediated transformation);

B) information, if applicable, on the DNA used to modify the plant (e.g. helper plasmids), including the source (e.g. plant, microbial, viral, synthetic), identity and expected function in the plant; and

C) intermediate host organisms including the organisms (e.g. bacteria) used to produce or process DNA for transformation of the host organism;

29. Information should be provided on the DNA to be introduced, including:

A) the characterization of all the genetic components including **marker genes, regulatory and other elements affecting the function of the DNA**;

B) the size and identity;

C) the **location and orientation** of the sequence in the final vector/construct; and

D) the **function**.

CHARACTERIZATION OF THE GENETIC MODIFICATION(S)

30. In order to provide clear understanding of the impact on the composition and safety of foods derived from recombinant-DNA plants, a comprehensive molecular and biochemical characterization of the genetic modification should be carried out.

31. Information should be provided on the DNA insertions into the plant genome; this should include:

A) the characterization and description of the inserted genetic materials;

B) the **number of insertion sites**;

C) the **organisation of the inserted genetic material** at each insertion site including **copy number** and sequence data of the inserted material and of the **surrounding region**, sufficient to identify any substances expressed as a consequence of the inserted material, or, where more appropriate, other information such as analysis of transcripts or expression products to identify any new substances that may be present in the food; and

D) identification of **any open reading frames** within the inserted DNA or created by the insertions with contiguous plant genomic DNA including those that could result in fusion proteins.

32. Information should be provided on any expressed substances in the recombinant-DNA plant; this should include:

A) the gene product(s) (e.g. a protein or an untranslated RNA);

B) the gene product(s)' function;

C) the phenotypic description of the new trait(s);

D) the level and site of expression in the plant of the expressed gene product(s), and the **levels of its metabolites** in the plant, particularly in the edible portions; and

E) where possible, the amount of the target gene product(s) if the function of the expressed sequence(s)/gene(s) is to alter the accumulation of a specific endogenous mRNA or protein.

33. In addition, information should be provided:

A) to demonstrate whether the arrangement of the genetic material used for insertion has been conserved or whether significant **rearrangements** have occurred upon integration;

B) to demonstrate whether deliberate modifications made to the amino acid sequence of the expressed protein result in changes in its post-translational modification or affect sites critical for its structure or function;

C) to demonstrate whether the intended **effect of the modification** has been achieved and that all expressed traits are expressed and inherited in a manner that **is stable** through several

generations consistent with laws of inheritance. It may be necessary to examine the inheritance of the DNA insert itself or the expression of the corresponding RNA if the phenotypic characteristics cannot be measured directly;

D) to demonstrate whether the newly expressed trait(s) are expressed as expected in the appropriate tissues in a manner and at levels that are consistent with the associated regulatory sequences driving the expression of the corresponding gene;

E) to indicate whether there is any evidence to suggest that **one or several genes in the host plant has been affected** by the transformation process; and

F) to confirm the identity and expression pattern of any new fusion proteins.

...

Assessment of possible allergenicity (proteins)

41. When the protein(s) resulting from the inserted gene is present in the food, it should be assessed for potential allergenicity **in all cases**. An integrated, stepwise, case-by-case approach used in the assessment of the potential allergenicity of the newly-expressed protein(s) should rely upon **various criteria used in combination** (since no single criterion is sufficiently predictive on either allergenicity or nonallergenicity).

As noted in paragraph 20, the data should be obtained using sound scientific methods. A detailed presentation of issues to be considered can be found in the Annex to this document.¹³

42. The newly expressed proteins in foods derived from recombinant-DNA plants should be evaluated for any possible role in the elicitation of gluten-sensitive enteropathy, if the introduced genetic material is obtained from wheat, rye, barley, oats, or related cereal grains.

43. The transfer of **genes from commonly allergenic foods** and from foods known to elicit gluten-sensitive enteropathy in sensitive individuals **should be avoided** unless it is documented that the transferred gene does not code for an allergen or for a protein involved in gluten-sensitive enteropathy.

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¹³ The FAO/WHO expert consultation 2001 report, which includes reference to several decision trees, was used in developing the Annex to these guidelines.

Compositional Analyses of Key Components

44. Analyses of concentrations of key components of the recombinant-DNA plant and, especially those typical of the food, should be compared with an equivalent analysis of a conventional counterpart grown and harvested under the same conditions. In some cases, a further comparison with the recombinant-DNA plant grown under its expected agronomic conditions may need to be considered (e.g. application of a herbicide)

Evaluation of Metabolites

46. Some recombinant-DNA plants may have been modified in a manner that could result in new or altered levels of various metabolites in the food. Consideration should be given to the potential for the accumulation of metabolites in the food that would adversely affect human health. Safety assessment of such plants requires investigation of residue and metabolite levels in the food and assessment of any alterations in nutrient profile. Where altered residue or metabolite levels are identified in foods, consideration should be given to the potential impacts on human health using conventional procedures for establishing the safety of such metabolites (e.g. procedures for assessing the human safety of chemicals in foods).

Food Processing

47. The potential **effects of food processing**, including **home preparation**, on foods derived from recombinant-DNA plants should also be considered. For example, alterations could occur in the heat stability of an endogenous toxicant or the bioavailability of an important nutrient after processing.

Information should therefore be provided describing the processing conditions used in the production of a food ingredient from the plant. For example, in the case of **vegetable oil**, information should be provided on the **extraction process** and any subsequent **refining steps**.

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SECTION 5 – OTHER CONSIDERATIONS

POTENTIAL ACCUMULATION OF SUBSTANCES SIGNIFICANT TO HUMAN HEALTH

54. Some recombinant-DNA plants may exhibit traits (e.g., herbicide tolerance) which may indirectly result in the potential for accumulation of pesticide residues, altered metabolites of such residues, toxic metabolites, contaminants, or other substances which may be relevant to human health. The safety assessment should take this potential for accumulation into account. Conventional procedures for establishing the safety of such compounds (e.g., procedures for assessing the human safety of chemicals) should be applied.

USE OF ANTIBIOTIC RESISTANCE MARKER GENES

55. Alternative transformation technologies that do not result in antibiotic resistance marker genes in foods should be used in the future development of recombinant-DNA plants, where such technologies are available and demonstrated to be safe.

56. **Gene transfer** from plants and their food products to gut microorganisms or human cells is considered a rare possibility because of the many complex and unlikely events that would need to occur consecutively. Nevertheless, the possibility of such events **cannot be completely discounted**.

...

58. If evaluation of the data and information suggests that the presence of the antibiotic resistance marker gene or gene product presents risks to human health, the marker gene or gene product should not be present in the food. **Antibiotic resistance genes used in food production that encode resistance to clinically used antibiotics should not be present in foods.** »