Safety/Risk Assessment of GMOs: GM Crops as an Example

Wendy Craig PhD
Biosafety Unit
craig@icgeb.org
Cartagena Protocol on Biosafety (CPB), 2000

- A major component of the Convention on Biological Diversity, 1992

- The CPB helps to ensure “an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on transboundary movements”

- Adopted on 29 January 2000, and entered into force on 11 September 2003 following the 50th instrument of ratification. Currently ratified or accessed by 143 countries (March 2008)

- Major GM non-CPB parties currently include: USA*, Argentina, Canada, Uruguay, and Australia*

* non-signatory countries
The CPB in Action

- The Protocol features 2 separate sets of procedures:
  - GMOs intentionally released into the environment (Advanced Informed Agreement)
  - GMOs used directly as food or feed or for processing (Article 11 of AIA)

- Both procedures are designed to ensure that recipient countries are provided with the information that they need for making informed decisions about whether or not to accept GMO imports

- Governments must base their decisions on scientifically sound risk assessments and on the precautionary approach

- Governments must also adopt measures for managing any risks identified by risk assessments, and they must continue to monitor and control any risks that may emerge in the future
An international consensus regarding the safety/risk assessment of GMOs and derived foods exists, based on the following guidelines:

**CODEX ALIMENTARIUS COMMISSION**

- Foods Derived from Biotechnology, 2004. Incorporating:
  - Principles for the Risk Analysis of Foods Derived from Modern Biotechnology, 2003;
  - Guidelines for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants, 2003;

**JOINT FAO/WHO EXPERT CONSULTATIONS**

- Safety Assessment of Foods Derived from Genetically Modified Animals, including Fish, November 2003
- Evaluation of Allergenicity of Genetically Modified Foods, January 2001
- Safety Aspects of Genetically Modified Foods of Plant Origin, June 2000
- Safety Assessment of Foods Derived from Genetically Modified Microorganisms, September 2001

**ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT**

- Safety Considerations for Biotechnology Scale-up of Crop Plants (1993)
- Recombinant DNA Safety Considerations (1986)
- OECD “Blue Book”

**UN ENVIRONMENT PROGRAMME**

Risk Analysis to Assist Decision-making

Stages of risk analysis:
key issue identification, risk assessment, risk decision-making and risk communication.
Progression through the system is not linear, but iterative. Feedback loops, although not included in this diagram, are an integral part of risk evaluation.

Green boxes - driven by society; Purple boxes - driven by science

(Safety/Risk) Assessment

- Recently, major stakeholders have begun to refer to the risk assessment of GMOs as an overall ‘safety’ assessment, in order to avoid the negative connotations that the public perceives with the word ‘risk’. However, this terminology has yet to be precisely defined and widely adopted.

- Risk assessment (RA) can be described as “a process of evaluation including the identification of the attendant uncertainties, of the likelihood and severity of an adverse effect(s)/event(s) occurring to man or the environment following exposure under defined conditions to a risk source(s)”

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An overview of general features of risk assessments of genetically modified crops

Wendy Craig · Mark Tepfer · Giuliano Degrassi · Decio Ripandelli
Before a GMO/LMO is released into the environment, a determination of the possible associated risks to the environment, including to human health, should be undertaken.

The pre-market safety assessment should be undertaken following a structured and integrated approach and be performed on a case-by-case basis.

It comprises hazard identification, hazard characterisation, exposure assessment and risk characterisation. The sequential steps in safety/risk assessment of GMOs identify characteristics which may cause adverse effects, evaluate their potential consequence, assess the likelihood of occurrence and estimate the risk posed by each identified characteristic.

The safety assessment of GMOs and derived products consists of two phases, i.e. a comparative analysis with their non-GM counterparts to identify differences, followed by an assessment of the environmental and food/feed safety or nutritional impact of the identified differences, including both intended and unintended differences.
‘Typical’ issues considered during a safety assessment

1 - Description of GMO
   - Characteristics of the donor and recipient organisms
   - Genetic modification and its functional consequences

2 - Environmental safety
   - Intended & unintended effects due to the modification of the recipient organism
   - Agronomic characteristics
   - Potential environmental impact

3 - Food/Feed safety
   - Compositional, nutritional characteristics
   - Potential toxicity & allergenicity of gene products, plant metabolites and whole GM plant
   - Influence of processing on the properties of food or feed
   - Potential for changes in dietary intake
   - Potential for long-term nutritional impact
1 - Description of GMO

- The **method of transformation**
  - *How was any Ti/Ri plasmid/vector disarmed?*
  - *Was any helper plasmid DNA/carrier DNA inserted?*

- Detailed **molecular characterisation** of the inserted DNA, as well as host genomic flanking sequences
  eg. the nature and source of vector used, incl. maps of all functional elements, restriction sites for probes, PCR primer positions & sequences, and a table of descriptions & functions, sources and construction, insertion site(s) and copy numbers of all inserted DNA (transgenes, regulatory sequences, vector backbone).

  - *Is the actual insert the INTENDED insert? Any partial inserts? Any deletions occurred?*
  - *Do any modifications occur that affect the product amino acid sequence?*
  - *Are 5' & 3' flanking/junction sequences given?* - information necessary for a) GM detection & traceability, and b) identification of any insertion/interruption of known ORFs, and potential to produce novel chimaeric proteins
  - *Are vector sequences present in the insert, especially origins of replication and antibiotic resistance genes?*
1 - Description of GMO

- Detailed characterisation, quantification and biological activity of the introduced proteins in various plant tissue, along with comparative analyses of sequence, immunology, toxicology and allergenicity with original source versions

- Is the new protein developmentally and stably expressed during the life cycle of the plant?

- Are any fusion proteins between fragmentary inserted donor sequences and recipient sequences created, and expressed?

- Have overall gene expression patterns been altered?

- Is the introduced gene functionally equivalent to an existing host gene? - eg. a herbicide tolerance transgene may be similar to host gene involved in aromatic amino acid synthesis, therefore analyses of protein content & amino acid composition triggered

- Is the new protein homologous to a) any known allergen or b) any known anti-nutritionals or lectins?

- Is the new protein more resistant to proteolytic enzymes than the non-GM counterpart?

- Detailed inheritance and stability studies

- Does the insert(s) segregate as predicted by its location?

- Is the introduced trait stable over a number of generations under representative environmental conditions?
2 - Environmental safety

Evaluates the biology of the conventional crop and assesses the impact of any deviation by GM plant

Does the GM plant differ from the parental or near isogenic non-GM plant in its biology? (eg. multiplication, dormancy, survivability, dispersal, out-crossing ability, stress tolerance, sensitivity to specific agents)

Is there any increase in horizontal gene transfer potential? - due to the presence of bacterial sequences (origins of replication, homologous sequences, etc.) in the insert, or changes in flower biology (extended flowering period, attractiveness to pollinators, change in fertility, etc.)
Crop Biology

Information normally given includes:

- Use as a crop plant
- Taxonomy and genetics
- Centre of Origin/Diversity and Cultivation
- Morphology, growth and development
  - Germination and vegetative growth
  - Reproductive development
  - Grain ripening
  - Competitors and symbionts
- Reproductive Biology
  - Pollination and pollen dispersal
  - Seed dispersal and dormancy
  - Vegetative regeneration
- Pests and diseases
  - Weeds
  - Insects and other invertebrate pests
  - Vertebrate pests
  - Diseases, parasites
- Toxicity (to humans, animals and other organisms)
- Allergenicity
- Weediness
  - Adaptation to different habitats
  - Out-crossing versus selfing ability
- Potential for gene transfer
  - Intraspecific gene transfer
  - Interspecific gene transfer
  - Gene transfer to other organisms
- References
2 - Potential environmental impacts

Evaluation undertaken of any potential environmental impacts concerning:

1. **Increased weediness or invasiveness** [due to characteristics of either GM crop or transgene(s)] - is a selective dis/advantage CONFERRD TO the GM plant?

   - Gene-flow by a) pollination of sexually-compatible relatives, and b) uptake of DNA from eaten or decayed GM material by microorganisms - should hybridisation or DNA uptake be possible, is a selective dis/advantage TRANSFERRED FROM the GM plant?

   - Non-target organisms and biodiversity - will the GM crop cause adverse effects on populations of non-target organisms?

   - Agricultural and cultivation practices - do the required cultivation practices for the GM crop plant have a negative impact on the environment?
The CSA is basically a two-tiered approach:

- **First step** - a thorough comparison (not limited to a simple comparison of major key nutrients or phenotypes) with the closely related conventional food counterpart to identify differences that may have safety implications

- **Second step** - comprises the toxicological and nutritional evaluation of the identified differences

Crop Composition

Information normally given includes:

- **Background**
  - Production; Consumption; Uses
  - Cooking/Processing; Industrial uses
  - Appropriate comparators for testing new varieties
  - Traditional characteristics screened by developers

- **Nutrients**
  - Carbohydrates; starch; dietary fibre
  - Proteins; amino acid composition
  - Lipids; Oils
  - Minerals; Vitamins
  - Key nutrients in animal feeds
  - Proximates (incl. moisture & total ash)

- **Anti-nutrients; secondary metabolites; toxicants**
  - Allergens
  - Digestive enzyme inhibitors
  - Lectins; Saponins; Tannins; Glycosides

- **Food use**

- **Feed use**
  - Identification of key products consumed by animals
  - Forage; Straw/Hay
  - Grain/seed
  - Hull; Bran; Meal
  - Whole plant
  - Identification of key products and suggested analysis for new varieties

- **References**
3 - Food/Feed safety

Discusses differences arising from the genetic components transferred to the host organism:

- **In comparative assessments, do the component concentrations fall within the natural range found in the non-GM counterparts?**

- **Are there any changes (including intended) to the concentrations of any toxins, anti-nutritional compounds and allergens?**

- **Are the characteristics of the end product modified by the applied processing and/or preserving technologies as compared with its non-GM counterpart?**

- **Will dietary changes (including intended) in consumer exposure to the end product occur?**

- **Post-market monitoring of GM food/feed - Is the product use as predicted/recommended? Are known effects & side-effects as predicted? Does the product induce unexpected side effects?**
ICGEB

The International Centre for Genetic Engineering & Biotechnology (ICGEB) is an international organisation dedicated to advanced research and training in molecular biology and biotechnology, with special regard to the needs of the developing world.

ICGEB promotes the safe use of biotechnology

It comprises 3 components:

- ICGEB - Trieste
- ICGEB - New Delhi
- ICGEB - Cape Town
The role of the **ICGEB Biosafety Unit** is to:

- **disseminate** as widely as possible **significant information** related to the biosafety issues raised through the use of products derived from modern biotechnology,

- **as well as to assist its Member States in their capacity** to identify, regulate, manage, and monitor those products within their own Countries.

www.icgeb.org/biosafety
The activities of the ICGEB Biosafety Unit are part of a fully interlocking package:

- to provide greater access to current scientific information (dissemination of information),

- to provide training in how to make best use of these data (capacity building - personnel), and

- to assist the identification of local gaps in information [required by the regulatory process but not already addressed by the scientific community] and help fill them (capacity building - local assistance)
BU Interacting activities

- **Capacity building**
  - Biosafety annual & regional workshops
  - Biosafety research at our Outstation in Ca’ Tron
  - Biosafety training & technology transfer
  - Construction of the Italian national BCH

- **Dissemination of information** ([www.icgeb.org/biosafety](http://www.icgeb.org/biosafety))
  - Biosafety Bibliographic Database (BBD)
  - Risk Assessment Searching Mechanism (RASM)
  - Biosafety Research Database (BiosafeRes)
  - WebPages and Biosafety News
  - Publications

- **International co-operation**
  - Voluntary Code of Conduct (1991)
  - Co-operation with UNIDO 🌍, UNESCO 🏛️, UNEP 🌍, FAO 🌍, and CBD-Biosafety Clearing-House (BCH)
  - Participation in the Inter-Agency Network for Biosafety (IANB)
Who the Biosafety Unit are:

Decio RIPA NDELLI
Head of Biosafety Unit

Ca’Tron (Outstation)
Mark TEPFER

Trieste
Wendy CRAIG
Giuliano DEGRASSI
Francesca FAROLFII
Alexander OCHEM

Rome (Italian BCH)
Anna RUSSO

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ICGEB Biosafety Unit

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