Valutazione del rischio sanitario per gli uomini e gli animali: la posizione dell’EFSA

Salvatore Arpaia – Claudia Paoletti

Gli OGM nella filiera agroalimentare: una rinuncia ragionata o un’opportunità non colta?
Roma, 10 Febbraio 2015
An organism is "genetically modified" if its genetic material has been changed in a way that does not occur under natural conditions through cross-breeding or natural recombination.

Defined by the European Union Directive 2001/18/EC (Art. 2)

In the EU, products that are, contain, or are produced from Genetically Modified Organisms (GMOs) must have an authorisation prior to entering the market.
EFSA’s role is to carry out scientific Risk Assessment on GMOs under two regulatory frameworks:

**Directive 2001/18/EC**

On the deliberate release into the environment of GMOs

**Regulation (EC) No 1829/2003**

On GM food and feed including derived products
WHAT EFSA CANNOT DO

- **Give authorisations** (for products such as GMOs, feed additives, food additives, pesticides etc)

- **Be responsible for food safety legislation** (sampling, labelling or other risk management issues such as co-existence measures)

- **Take charge of food safety/quality controls**
The GMO Panel (19 external experts) for a 3-y mandate
- elaborates guidance documents
- delivers scientific opinions on applications for market authorisation regarding GMOs

40 Ad-hoc experts support the GMO Panel in Working groups (4 standing WG and several temporary WGs)

15 GMO Unit scientists provide support to the GMO Panel and its Working Groups
EFSA GMO PANEL EXPERTISE

**MOLECULAR CHARACTERISATION**
- biochemistry
- molecular biology
- genetics
- plant breeding

**ENVIRONMENTAL RISK ASSESSMENT**
- plant biology
- ecology
- agronomy
- entomology
- biometrics & statistics

**FOOD FEED SAFETY**
- toxicology
- immunology
- nutrition & animal feed
- food chemistry
- biotechnology

Ad-hoc experts in new techniques, microbiology

Ad-hoc experts in food sciences, animal pathology

Ad-hoc experts in pesticides, natural toxins, environmental monitoring

- 15 EFSA staff scientists
- 40 ad hoc experts
- 210 MS experts from 108 organisations and authorities of EU member states
ROLES UNDER REG (EC) NO 1829/2003:
GM FOOD AND FEED INCLUDING DERIVED PRODUCTS

Applications of GM plants with scope cultivation:
One Member State performs initial ERA

GMO application (via a Member State)

Overall Opinion

European Commission: draft decision

Member States and European Commission:
Decision to authorize or not to authorize in Standing Committee

All applications: Consultation with all Member States via GMO EFSAnet

RISK ASSESSMENT

RISK MANAGEMENT

Public consultation
### SCIENTIFIC OPINIONS ON APPLICATIONS

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EFSA Guidance documents

- Provide guidance for applicants how to prepare and present the applications
- Detailed guidance needed as only full dossiers are considered
- Based on internationally agreed principles and protocols (Codex Alimentarius, OECD)
- Regularly updated
- Undergo public consultation
SELECTED EFSA’S GUIDANCE DOCUMENTS ON GMOs

- Risk assessment of food and feed from GM plants (2011)
- Post-Market Environmental Monitoring (PMEM) (2011)
- Environmental Risk Assessment (ERA) of GM Plants (2010)
- Food and feed RA from GM animals and GM animal health and welfare (2012)
- Environmental Risk Assessment (ERA) of GM animals (2013)

NEW IMPLEMENTING REGULATION ON GM PLANT APPLICATIONS FOR FOOD AND FEED USE

Regulation (EU) No 503/2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003

• Mandatory from 8 December 2013
• Defined the scientific information requirements to be provided in applications for GM plant-derived food and feed under Regulation (EC) No 1821/2003
• The EFSA Guidance for risk assessment of food and feed from GM plants (2011) is only in place for applications submitted before 8/12/2013
• Reflects the EFSA GD to a large extent but contains additional mandatory elements
NEW IMPLEMENTING REGULATION ON GM PLANT APPLICATIONS

Novel elements in IR (EU) No 503/2013

- **90 day feeding study with whole food/feed** mandatory for all single events
  - A review of this requirement is foreseen by 2016. The Commission will perform this review based on new scientific information such as the outcome of the EU project GRACE (GMO Risk Assessment and Communication of Evidence) (see Art. 12, IR 503/2013).

- **re-sequencing of DNA inserts and their flanking regions** in GM plants containing stacked events
  - To be compared with the nucleotide sequence of the respective single events

- **Quantitative measurement of allergens** in the frame of compositional analysis as referred to in relevant OECD documents
Risk assessment methodology and principles

- Science- and evidence-based
- Case-by-case
- Step-by-step (6 steps)
- Comparative approach (GM vs non-GM)
KEY PRINCIPLES OF GMO RISK ASSESSMENT

COMPARATIVE APPROACH

comparison between the GMO (and derived products) and its conventional counterpart

Assessment of the identified differences regarding:

- Environmental impact
- Food/Feed safety
- Nutritional impact

- **Intended effects**: those occurring because of the genetic modification
- **Unintended effects**: additional effects which were NOT the objective of the genetic modification
GMO RISK ASSESSMENT OF GM FOOD AND FEED

Molecular Characterisation

- Genetic modification
- Characteristics of the GM plant

Food and Feed safety

- Compositional and agronomic assessment
- Toxicological assessment
- Allergenicity assessment
- Nutritional assessment
Traditionally cultivated crops are well known (Concept of familiarity) and have gained a history of safe use for the environment, consumers and animals.

These crops can serve as a baseline for the environmental and food/feed safety assessment (Concept of Substantial Equivalence or Comparative Safety Assessment).

Reg. EC1829/2003:
...show that the characteristics of the food are not different from the those of its conventional counterpart...
(having regarded natural variation)
Choice of comparator

• **Conventional counterpart:**
  - non-GM isogenic variety (vegetatively propagated)
  - genotype as close as possible (sexually propagated)

• **Non-GM reference varieties:** those in the field to establish ranges of natural variation (equivalence test)

*EFSA GD on selection of comparators (2011)*
Design for field trial: minimum requirements

- GM, non-GM comparator & reference varieties are all randomised and replicated at each site.

- must be at least 8 sites, over one or more years.

- must be the same GM, non-GM comparator at each site.

- may be different reference varieties at each site.

- must be at least 6 reference varieties over all the sites.

EFSA FF GD (2011)
Difference & Equivalence test

Test of Difference:
To verify whether the GMO is different from the non-GM comparator (identification of possible hazard)

Test of Equivalence:
To verify whether the GMO is equivalent to appropriate reference varieties (natural variation)

When differences or lack of equivalence are identified their biological relevance must be further assessed.

1. Starts with evaluation of the **novel proteins** due to the genetic modification (possible toxic effects, comparative approach)

2. Further evaluation of the **whole food/feed** is hypothesis driven, depending upon:
   - Evaluation of the novel protein
   - Outcome of the comparative assessment

**Safety of whole food/feed:**

- **When**: if composition of the food/feed is substantially modified, or if possibility of unintended effects
- **What**: 90-day oral toxicity study in rodents according to the principle of OECD guideline (compulsory for single events since 2013)
Allergenicity assessment

Newly expressed protein

• Aminoacid sequence homology comparison

• In vitro digestibility tests (e.g. using pepsin): physiological conditions to be considered.

Whole GM plant

• Edible components and the pollen of GM plants (i.e. covers both food and respiratory allergy risk)

• Information on the prevalence of occupational allergy in workers or farmers

Conclusions:

Indicate the likelihood of the novel protein to be allergenic
Indicate if the GM plant food/feed is more allergenic than the comparator

EFSA FF GD (2011) + EFSA allergenicity opinion (2010)
Nutritional assessment

- Newly expressed protein
  - Food/feed
- New components (e.g. acetylated amino acids)
- Altered concentrations of natural components

Tables of food composition (e.g. FAO, INRAN)
Within the frame of the RA approach described in the GD, the GMO Panel requires a CASE-by-CASE approach:

- In the context of the intended uses of the GM product.
- In light of the evaluation of all available scientific information (not only what is delivered by the applicant in the application).
- In case the Panel needs more specific information: the applicant is asked for additional information.
International Context

EFSA does not work in isolation!

- European Commission
- **OECD**: Organisation for Economic Co-operation and Development
- **FAO/WHO**: CODEX Alimentarius

**Common foundation:**
the comparative approach *(Codex Alimentarius, 2003)*

Different countries = different levels of requirements. EU has the most stringent ones!
Thank you for your attention!

www.efsa.europa.eu

All Guidance documents and opinions available!