Draft Guidance on Selection of Comparators for the Risk Assessment of GM Plants

Chapter 4

Cases where alternative approaches in the comparative risk assessment may be required

Alternative approaches = Safety Assessment per sé

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In case no Comparator(s) are available: Safety Assessment per sé

- GM plant derived food/feed with complex compositional alterations
  - New) fats, oils, lipids
  - Carbohydrates
  - Vitamins
- GM plants with improved environmental responses:
  - Drought tolerance
  - Salt tolerance

- **The extent and complexity of molecular and compositional alterations indicates whether a strict comparative analysis can be made**

- If no comparator available:
  - 'normal' , 'full' safety assessment
  - further detailing safety assessment per sé

Issues raised at the Public Consultation

- The assessment of GM plants with *complex* modifications may provide more difficulties for selecting the *appropriate tes*ts for assessment than the non- availability of a conventional counterpart.

- It is even more important that respective studies are provided demonstrating that the GMO and the derived products do not possess the potential for sub-chronic, chronic, long-term, reproductive or developmental toxicity.

Issues raised at the Public Consultation

- Inappropriate example of GM oilseed rape with high levels of lauric acid:
  - palm kernel or coconut oil are additional comparators, NOT the principal ones

- ERA of *unintended* effects of GM plant with enhanced nutritional properties (attracting a range of phytophagous species and possible increased levels of pest infestation) is covered in the ERA Guidance Document

Safety Assessment per sé

- Characteristics of donor organisms and recipient plant
- Genetic modification and its functional consequences
- Agronomic, phenotypic analysis
- Extensive compositional analysis per sé
  - Possible comparisons with other food/feed

Safety Assessment per sé

- Potential toxicity and allergenicity of new gene products (proteins, metabolites) and of endogenous compounds:
  - Threshold levels, ADIs etc
- Potential toxicity and allergenicity of the whole GM plant derived food/feed
- Dietary intake and potential for nutritional impact
- Influence of processing and storage

Toxicity Tests for Single Substances

- ***Case-by case selection of Toxicity Tests***

- *In vivo* tests in laboratory animals (OECD test guidelines, European Commission Directives)

    - *Single dose toxicity testing*
    - *Repeated-dose toxicity testing including 28/90-day oral toxicity, chronic toxicity, carcinogenicity*
    - *Reproductive and developmental toxicity testing*
    - *Immunotoxicity testing*

- Specific tests

    - *In vitro tests*
    - *In silico search for sequence homology*
    - *In vitro stability tests of proteins under gastro-intestinal conditions*
    - *Genotoxicity tests*
    - *Immunochemical cross-reactivity tests*
    - *Profiling technologies*

- Studies under (GLP) described in Council Directive 2004/10/EC

90-Day Rodent Feeding Trials for the Safety and Nutritional Assessment of Whole GM Food and Feed

efsa
European Food Safety Authority

- To check in an animal model whether the GM plant derived food or feed does not induce adverse effects and is nutritious
- Hypothesis- driven studies of possible antagonistic interactions between food components and of possible matrix effects
- Protocol adapted from the OECD 90-day rodent toxicity study, Guideline 408 (OECD, 1998), EFSA Opinion Scientific Committee, 2011 in progress

Conclusion

- Safety assessment per sé of GM crop derived food/feed relies on the assessment of the specific characteristics of the food/feed rather than on comparisons

- Analytical and toxicological tools are available

- Product- based Assessment rather than Technology-based Assessment