

Introduction

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1 Scope of the document

This document describes the elements needed for the safety assessment of foods and feeds derived from genetically modified crops. This document does not address environmental, ethical or socio-economical aspects of the marketing of these foods and feeds, but considers the aspects with relevance to human or animal health.

This document provides guidance to notifiers and biosafety assessors as to which extent studies have to be carried out following a case-by-case approach for the evaluation of genetically modified food and feed crops. This guidance document is not a static data package, but should be considered along with newly evolving scientific knowledge and technology.

The scientific aspects and the presentation of information in the dossier should fulfil the requirements of the ongoing legislations and recommendations as specified in section 4 of this chapter. This document complements these requirements by providing more detailed guidelines for the safety assessment of foods and feeds derived from genetically modified crops.

2 Genetically modified food and feed crops

The first transgenic crops destined for human or animal consumption which are currently in use or close to commercialisation, have been modified for improved agronomic properties. These so-called first-generation crops have been altered to confer resistance to common pests or to introduce tolerance to selected herbicides for better weed control. To date only a few crops have been modified for improved quality traits. These traits will continue to be targets of next-generation products to obtain foods and feeds with enhanced or altered nutritional properties. Although these products have not entered the market yet, the safety assessors should be aware of their possible rapid arrival and the possible implications for their safety assessment approach.

This document addresses in first instance the safety evaluation of first-generation crops, but also takes into consideration the information that could be needed for the safety assessment of next-generation products. The need for additional tests could however be extended if, once these products are submitted for authorisation, experience shows that the available tests are not enough for a thorough safety assessment.

3 Food versus feed safety assessment

Many crops (or by-products of these crops) are used for human consumption as well as for livestock feeding. The food and feed safety assessment of such crops will consequently follow the same strategy, starting with a thorough description of the genetic modification, followed by the assessment of the potential toxicity and allergenicity of the newly expressed gene products and metabolites, and finally, the evaluation of the nutritional aspects of the genetically modified crop.

On the implementation level there can however be some differences between the food and feed safety assessment. The necessary parameters to be measured can be different, as well as the methods of analysis to be used. Furthermore, the safety assessment of animal feeds should consider, besides any risk to the animals consuming the feed, any indirect risk to the consumer of animal products.

4 Food and feed safety regulations

Directive 90/220/EEC put in place a step-by-step approval process on a case-by-case assessment of the risks to human health and the environment of any genetically modified organism or product consisting of or containing genetically modified organisms before it can be released into the environment or placed on the market (EU, 1990). Since 17th October 2002 Directive 90/220/EEC is superseded by Directive 2001/18/EC (EU, 2001a). The principles for the environmental risk assessment are laid down in Annex II of Directive 2001/18/EC and guidance notes to this annex are provided by the Decision 2002/623/EC (EU, 2002).

Risk assessments carried out under Directive 2001/18/EC address risks to human and animal health after exposure to the genetically modified organism concerned, including incidental consumption; it does not address the use in food of genetically modified organisms or their products. Genetically modified food destined for human consumption is currently regulated by Regulation (EC) 258/97 on Novel Foods and Novel Food Ingredients (EU, 1997a). The scientific aspects and the presentation of information necessary to support applications for the placing on the market of genetically modified foods are provided by the recommendations 97/618/EC (EU, 1997b). There is currently no specific regulation governing the use of genetically modified feed and the authorisation occurs in accordance with Directive 2001/18/EC. In July 2001, the European Commission adopted a proposal for a Regulation of the European Parliament and of the Council on genetically modified food and feed (EU, 2001b). This draft regulation provides authorisation on genetically modified organisms for food and/or feed use, food and/or feed containing or consisting of genetically modified organisms, as well as food and/or feed produced from or by genetically modified organisms. From the date of application of the genetically modified food and feed regulation, the provisions laid down in this regulation will repeal the provisions in the Novel Food regulation on genetically modified foods.

5 Introduction to food and feed safety assessment

New varieties obtained through traditional breeding methods are generally recognised as safe and continue to enter the market. These varieties are evaluated by breeders for agronomic and phenotypic characteristics, but the genetic and

metabolic changes associated with traits such as disease and pest-resistance, introduced by conventional techniques from wild species, are rarely characterised in detail. Despite of the possible occurrence of undesirable new combinations of genes by conventional breeding, a formal food safety assessment is not required for conventionally bred crops.

The genetic material in crops obtained through genetic modification can also be altered in a way that does not occur naturally by mating or natural recombination. Genetic modification also allows selected individual genes to be transferred from one organism into another, also between non-related species. Crops obtained through genetic modification have, in contrast to conventional obtained crops, to be subjected to rigorous food and feed safety testing procedures.

In conventional breeding, as well as in genetic engineering, rearrangements or transfer of genes can result in the expression of one or more new constituents in the crop, or change the expression of existing constituents, either positively or negatively. It should therefore be more appropriate if the safety assessment has to be carried out regardless the method of modification used. The use of a particular method of breeding or genetic engineering does not give the resulting plant a particular property. Its properties will depend on what genes are transferred or modified.

This document is in first instance designed for foods and feeds derived from genetically modified crops.

6 Safety assessment strategy

The elements to be considered in the safety assessment strategy concern the characterisation of the genetic modification, the evaluation of the possible toxicity and allergenicity of gene products and metabolites, as well as the consideration of the nutritional aspects of the food or feed in question. These aspects are dealt within separate chapters further on in the document.

Contrary to the risk evaluation of food additives, residues of pesticides and medicinal products, for which the substance to be tested is well characterised, of known purity and of no particular nutritional value, foods and feeds do contain complex mixtures of compounds. The safety evaluation of a single, well-defined chemical is virtually impossible and due to their effect on nutritional imbalances, the application of traditional toxicological testing and risk assessment procedures to whole foods and feeds is not possible. A more focused approach is required for the safety assessment of foods and feeds derived from plants, including genetically modified crops.

The food or feed derived from the genetically modified crop is in first instance compared with its conventional counterpart to establish the extent of equivalence¹. Following a holistic approach this comparison implies for instance the characterisation of the genetic modification and the analysis of the composition. Based on the identified differences, the genetically modified food or feed will be

¹ Establishing the extent of equivalence is known as the concept of *substantial equivalence*. This concept has attracted some criticism, partly due to the misperception that substantial equivalence is the endpoint of a safety assessment, rather than the starting point (WHO/FAO, 2000; OECD, 2001).

subject to further safety assessment. Different outcomes of the comparative approach can be envisaged (EU, 1997b):

- substantial equivalence can be established to its conventional counterpart; the need for further testing should be investigated on a case-by-case basis.
- substantial equivalence can be established except for a single or few specific traits of the genetically modified crop, in which case any further assessment of safety should focus specifically on these traits; safety tests include for instance toxicity and allergenicity testing and analysis of the nutritional impact of the genetically modified food or feed in the diet.
- neither partial nor total substantial equivalence can be established; on a case-by-case basis, the wholesomeness of the whole food or feed has to be assessed using an appropriate combined nutritional-toxicological approach.

7 References

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