

Safety Evaluation of Novel Foods: A European and International Perspective (From European Food International Council)

In the past, foods prepared and used in traditional ways have been judged safe on the basis of long-term experience, even when they contain natural toxicants (e.g. solanin in potatoes) or anti-nutritional substances (e.g. phytate in soya beans). In today's scientific language we would say that a food is considered safe when we are reasonably certain that it will cause no harm if it is used as intended, under the anticipated conditions of consumption.

The early days of Novel Foods

During the 1970s, the pace of advances in food technology increased rapidly. New products and processes were developed, especially in response to a perceived shortage of food, and particularly animal protein. Developments included methods to produce protein foods from new plant and microbial sources and to use textured plant proteins as meat analogues and extenders.

At that time, many countries had experience in evaluating the safety of food additives and contaminants. However, there was little experience in the safety evaluation of new foods or food ingredients ("novel foods") because food additives are present in very low levels compared to food ingredients. Techniques available for the safety evaluation of well-defined substances were thus not easily applicable to novel foods.

In an attempt to ensure systematic safety evaluation of novel foods, the Protein Advisory Group of the United Nations (PAG/UNU) issued Guidelines for the Preclinical Testing of Novel Sources of Protein and Guidelines for the Human Testing of Supplementary Food Mixtures in 1972. These Guidelines focused on novel microbial proteins. They were revised and re-issued by the United Nations University in 1983, when their scope was expanded to cover Preclinical Testing of Novel Sources of Food and Human Testing of Novel Foods.

Novel foods were defined as foods not previously eaten by humans. The guidelines identified the main categories of information needed to evaluate the safety of novel foods as well as some of the problems with testing their safety.

Some feeding challenges of food safety evaluation

The usual way to test the safety of a substance in food (e.g. additives or contaminants) is to feed it to laboratory animals. After establishing the level in the diet at which animals show no adverse effects, the maximum level of intake from human food is estimated to ensure that there is a large safety margin (often more than 100 times). This is possible because the substances can be included in animal diets at levels corresponding to many times their anticipated level in human food.

This approach may not be appropriate for evaluating the safety of novel foods or food ingredients since these are often intended for use in human foods at levels that are much higher than those for additives. As they may reach ten per cent or more of the food, it is impossible to include them in animal diets at levels one hundred times higher.

Furthermore, even if it was possible to include the novel food in animal diets at levels above ten or twenty percent, and the animals would eat the food, it could severely upset the nutritional balance of the diet. Many novel foods, like conventional foods, are complex mixtures of many substances including macro- and micro-nutrients. This makes it difficult to determine the cause of any effects observed during animal studies. This is why new approaches to safety assessment were developed for novel foods.

A new approach is developed

Innovations in the food industry during the 1970's were accompanied by increasing consumer interest in food safety and a recognition that it was inconsistent to require extensive testing for food additives but not for foods or food ingredients that might be consumed at much higher levels.

In response to reports during the period 1974-1980 on novel protein foods, the UK Government introduced a notification scheme for novel foods in 1984 that supplemented general safety provisions in food law. Under this scheme, safety data for novel foods were assessed by an independent committee before the food was marketed. This was the first time that a government had introduced specific provisions for novel foods and it was followed by a regulation issued in the Netherlands for protein food ingredients. The UK committee published Guidelines for the Testing of Novel Foods in 1984. These guidelines advocated a case by case approach and paralleled the approach in the earlier PAG/UNU guidelines. As experience with the safety evaluation of novel foods in the UK grew, further editions of the UK guidelines were published. These were more detailed and included structured approaches to ensure that developers provide adequate data.

Special focus on genetically modified foods

In the early 1990s it became clear that developments in gene technology would have significant implications for the food supply, particularly in terms of their potential to increase the quantity and quality of available foods. Several international organisations and

regulatory agencies in individual countries began developing guidelines for assessing the safety of foods derived from genetically modified organisms ("genetically modified foods"). Foremost amongst these were:

- the World Health Organisation (WHO),
- the UN Food and Agriculture Organisation (FAO), and
- the Organisation for Economic Cooperation and Development (OECD).

The aims of these organisations are, respectively:

- the highest possible standard of health for all,
- the provision of safe food for all, and
- the development of the world economy.

In spite of the different aims and backgrounds of the three organisations, their reports propose a similar approach to the safety assessment of genetically modified foods.

They advocate comparing a genetically modified food to an equivalent conventional food to establish its safety. If the comparison shows no differences, then the genetically modified food is considered to be as safe as its counterpart.

The counterpart is usually the parent strain used to produce the genetically modified organism or a closely related edible strain. If the comparison reveals differences (e.g. in agronomic characteristics or chemical composition), these should be the focus of a more detailed safety evaluation. This may require animal tests of chemical components responsible for the difference but not, usually, of the whole food.

If it is not possible to fully characterise the differences between the genetically modified food and its counterpart, (e.g. if there is no counterpart or if there are many differences), this does not mean that the genetically modified food is unsafe. However, a more extensive evaluation will be required to establish safety and this may involve animal testing of the whole genetically modified food.

The comparative approach or substantial equivalence

The comparative approach is particularly suitable for food organisms in which only a small number of traits have been modified (e.g. to delay softening in tomatoes or to reduce pests on soya) since these will usually have small, predictable differences from their parents.

The advantages of the comparative approach are: the comparator defines a standard that meets the acceptable level of safety, it is practicable, and the animal tests are restricted to those situations where they are of real value. On the other hand and this is true for all safety testing, the approach does not guarantee absolute safety.

Long term testing may be required for novel components introduced through genetic modification and for the genetically modified food or any novel food when the long-term safety of the comparator has not been established. Thus, the safety of the genetically modified organism is equivalent to that of the comparator plus that of any differences between it and the comparator.

Many regulatory agencies have incorporated the comparative approach into their guidelines for the safety testing (risk assessment) of genetically modified foods, including Australia, New Zealand, Canada, the European Union, Japan and the United States. However, the regulatory frameworks (risk management) vary significantly between countries. In the US, genetically modified foods are not subject to specific food safety regulations although the Food and Drug Administration has issued guidelines for the safety evaluation of all new plant varieties including those developed using genetic modification. The developers inform the agency that they intend to introduce the genetically modified food into the market and provide the data that leads them to conclude that it is safe. In the EU, genetically modified foods are subject to specific food safety regulations and most require regulatory approval before they can be marketed.

The European legislation

Within the EU, genetically modified foods have been controlled since 1997 through the EU Regulation on Novel Foods and Novel Food Ingredients. The Regulation covers foods and food ingredients that have no significant history of consumption in the EU and that fall into one of the following categories:

- foods/ingredients consisting of/or containing genetically modified organisms,
- foods/ingredients produced from genetically modified organisms,
- foods/ingredients with a new or intentionally modified molecular structure,
- foods/ingredients consisting of/or isolated from micro-organisms, fungi or algae,

- foods/ingredients consisting of/isolated from plants and food ingredients isolated from animals except foods/ingredients obtained by traditional propagating or breeding practices and having a history of safe food use, or
- foods/ingredients obtained using a novel process that gives rise to significant changes in structure or composition that affect the nutritional and safety characteristics of the food/ingredient.

Although developed initially to facilitate the safety evaluation of genetically modified foods, the comparative approach to food safety evaluation has also been extended to other classes of novel foods.

Food additives, flavourings and extraction solvents used in food production are not within the scope of the Regulation; these are covered by other legislation.

Formal approval prior to consumption

The EU Regulation requires that all novel foods (including genetically modified foods) are safe, that there are no misleading claims associated with them, and that they are not less nutritious than the foods that they might replace in the diet. To ensure that these requirements are met, most novel foods must undergo a formal approval process before they can be marketed in the EU. An application must be submitted to the Member State where the novel food will first be marketed, including data to demonstrate its safety and labelling proposals. Certain categories of novel food (but not foods/food ingredients consisting of or containing genetically modified organisms) are exempted if it can be shown that they are substantially equivalent to their counterparts.

The European Commission's Scientific Committee for Food (SCF) recommends that the following data be provided to support an application for approval of a novel food under the EU Regulation:

- the specification of the novel food,
- effects of any production process,
- history of the organism used as the source of the novel food,
- anticipated intake or extent of use,
- information from previous human exposure to the novel food or its source,
- nutritional information,
- toxicological information, and
- microbiological information.

In addition, the following data is required for genetically modified foods:

- effect of the genetic modification on the properties of the host organism,
- genetic stability,
- specificity of expression of novel genetic material,
- likelihood of transfer of genetic material from genetically modified micro-organisms, and
- ability of genetically modified micro-organisms to survive in and colonise the human gut.

The SCF guidelines include structured schemes to help identify the necessary information in each category. These schemes emphasise the need for comparative data to support the toxicological and nutritional evaluation of novel foods and importance of focusing for further studies on the implications for the consumer of differences between the novel food and its counterpart. Thus, the presence of new toxins, anti-nutritional factors or allergens (or increased levels of existing toxins, anti nutritional factors or allergens) will indicate the need to assess their safety implications. If the novel food is not nutritionally equivalent to the foods that it might replace, then the nutritional impact of the introduction of the novel food must be assessed.

Conclusion

Those seeking to manage potential food safety risks from novel foods have been in the unusual position of regulating developments before they become reality. Application of conventional risk assessment strategies to novel foods raises considerable practical problems. The comparative approach to food safety assessment is flexible and should be able to adapt to future developments and ensure that our novel foods are safe.

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Safety Evaluation of Novel Foods Reading List

Strategic approaches:

- Strategies for Assessing the Safety of Foods Produced by Biotechnology, World Health Organization, Geneva (1991)
- Safety Evaluation of Foods Derived by Modern Biotechnology - Concepts and Principles, Organisation for Economic Cooperation and Development, Paris (1993)
- Health Aspects of Marker Genes in Genetically Modified Plants, World Health Organization - Food Safety Unit, Geneva (1993)
- Aquatic Biotechnology and Food Safety, Organisation for Economic Cooperation and Development, Paris (1994)
- Application of the Principles of Substantial Equivalence to the Safety Evaluation of Foods or Food Components from Plants Derived by Modern Biotechnology, World Health Organization - Food Safety Unit, Geneva (1995)
- Food Safety Evaluation, Organisation for Economic Cooperation and Development, Paris (1996)
- The Safety Assessment of Novel Foods, Food and Chemical Toxicology 34 (10) 931-940 (1996)

Guidelines:

- PAG/UNU Guideline No. 6: Preclinical Testing of Novel Sources of Food, UNU Bulletin 5 (1) 60-63 (1983)
- Guidelines on the Assessment of Novel Foods and Processes, Report on Health and Social Subjects No. 38, HMSO, London (1991)
- Commission Recommendation of 29 July 1997 concerning the scientific aspects and the presentation of information necessary to support applications for the placing on the market of novel foods and novel food ingredients and the preparation of initial assessment reports under Regulation (EC) No 258/97 of the European Parliament and of the Council, Official Journal of the European Communities, L 253/1-36 (1997)

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