



FOOD AND AGRICULTURE ORGANIZATION
OF THE UNITED NATIONS
WORLD HEALTH ORGANIZATION



3442 2

JOINT FAO/WHO CONFERENCE ON FOOD
STANDARDS, CHEMICALS IN FOOD AND
FOOD TRADE

Rome, Italy 18-27 March 1991

DISTR.: LIMITED
DISTR.: LIMITEE

WHO/HPP/FOS/91.1
Original: English



Assessment of Biotechnology in Food Production
and Processing
as Related to Food Safety

Prepublication copy containing unedited excerpts of the report of a
Joint FAO/WHO Consultation, Geneva 5-10 November 1990.

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1. OPENING REMARKS

A Joint FAO/WHO Consultation on the Assessment of Biotechnology in Food Production and Processing as Related to Food Safety was held in Geneva from 5 to 10 November 1990. The Consultation was opened by Dr Rochon, Director of the Health Protection and Health Promotion Division of WHO. In welcoming participants on behalf of the Directors-General of FAO and WHO, Dr Rochon drew attention to the long history of the application of biotechnology to food production and processing. This went back more than eight thousand years and the food industry is one of the oldest users of biotechnological products and processes.

Since the nineteenth century, Dr Rochon said, the science of biotechnology has developed more rapidly than previously and particularly so over the last decade. Whilst there are many applications of biotechnology in areas such as drugs, the new technologies also have the potential to revolutionize the world's food supply. Enormous improvements are possible both in the quantity and quality of food available. Contemporary techniques of genetic modification make it possible to speed up the classical processes of plant and animal breeding and enable interspecies gene transfers not possible by classical methods.

Dr Rochon predicted an enormous impact of biotechnology on providing food for the world's rapidly increasing population by changing the character of food sources. The challenge was to develop appropriate safety assessment procedures to ensure that these new food sources would be safe for human consumption. An international consensus regarding the safety assessment of foods derived from biotechnology would be a strong foundation for consistent national regulatory activities and it is hoped that the Consultation will be a valuable initiative in this direction.

Biotechnology raises a number of important non-scientific issues including ethics, consumer perception and food labelling, which will need to be taken into account by the national regulatory agencies. Such issues were, however, outside the remit of the Consultation which would confine its activities to the scientific issues of safety assessment.

In his reply, Dr Miller, Chairman of the Consultation, emphasized the need for a strong science base for any national and international regulatory activities if biotechnology were to move forward. A very careful balance would be necessary to ensure that any possible problems were not understated whilst at the same time ensuring that the public was not alarmed by overstating any perceived problems; if ignorance existed, it would need to be acknowledged.

The Consultation was established to develop appropriate safety assessment strategies and procedures for the application of biotechnology to food production and processing, and it adopted the objectives, terms of reference and definitions attached at annexes 2 and 3. For a definition of

the other terms used in this report, attention is drawn to the glossary at the end of this report. The Consultation noted that the definition of biotechnology applied equally to classical and modern techniques, underpinning the fact that with regard to safety there are no fundamental differences between traditional and contemporary products from biotechnology. It agreed, therefore, that it was appropriate that the same broad principles of safety assessment should apply to the products of the old and new biotechnologies.

In addition to its direct application to food production and processing, biotechnology also has applications in the production of veterinary drugs, pesticides and other products used in agriculture, and also in the development of improved methods for use in food analysis. Such aspects, which are outlined in sections 3.1.4 and 3.4 of this report, are of significance to food safety. However, it was agreed that such aspects would not be considered in detail by the present Consultation.

Environmental aspects of biotechnology are also important but the Consultation agreed that these would not be dealt with directly in this report as these concerns are being dealt with elsewhere. The notification requirements which precede the deliberate introduction into the environment of genetically modified food organisms; (e.g., microbes, plants and animals) will usually precede any consideration of food safety. Much of the data necessary for the examination of these environmental aspects will also be of value in assessing food safety: in particular, information on the characteristics of the host and donor organisms, genetic insert and vector. Environmental information on genetically modified plants is particularly relevant to food safety as it also applies to the potential transfer of genetic material to other food crops through pollen transfer.

2. INTRODUCTION

Biotechnology has been linked with food production and processing since time immemorial. Almost every ingredient used in the production of food has as its source a living organism, i.e., animal, plant or micro-organism. The food sources available to early man, whether plant or animal, had evolved through natural selection. Genetic diversity arising from spontaneous genetic changes, including recombination, mutation and reproductive isolation, was exploited when the early farmers began to save the seeds from their best crops for later sowings and to use the best animals for breeding.

Even before the laws of independent assortment were discovered by Mendel in the 1860s and rediscovered in the early part of this century, their significance was recognized and applied empirically in selective breeding programmes. The simple procedure of maximizing reproductive efficiency of organisms with advantageous phenotypes, while limiting reproduction of organisms with undesirable traits, led to profound improvements in productivity of many animal and plant species. With the

discovery of Mendel's laws, these practices were applied in a more formal scientific manner.

Mendel's work has been exploited by those developing new strains of organisms for use in food production or processing. Although very considerable advances have been made, there are limits to what can be achieved by conventional breeding and strain selection. The process is slow; limits are imposed by the genetic diversity of the parent organisms, it is often unpredictable, and lengthy back-crossing may be necessary to remove undesirable traits introduced along with the desirable ones.

The value of breeding and selection techniques can be improved by increasing the genetic diversity within the gene pool of the parent organisms. Muller, working on *Drosophila* in the 1930s, showed that X-rays could have a point effect on a single gene within the organism. Other forms of radiation and certain chemicals have been found to have a similar effect. Mutants induced through these treatments have been used successfully in plant breeding, where it is possible to produce large numbers of progeny from plants grown from treated seed. Screening identifies useful mutants and these can be incorporated into breeding programmes.

The plant breeder's task has been eased considerably in recent years by the integration into breeding programmes of plant cell culture techniques.

In food plants, many of the traits which are the targets for change are controlled by more than one gene and it will be many years before these systems are fully understood and capable of being genetically modified. The strategy of locating quantitative trait loci (QTLs) with restriction fragment length polymorphisms (RFLPs) employs the fact that DNA sequence polymorphisms, reflected as alteration in the distribution of restriction endonuclease cleavage sites, can often be identified either within or very close to a desired gene. In the tomato, for example, genes affecting fruit mass can be identified by crossing a tomato with high fruit mass with another variety of tomato that has many polymorphic differences in restriction enzyme sites. Progeny plants can then be screened with probes known to be derived from each plant chromosome, and a matrix constructed in which the presence of a specific chromosome from the parent with high fruit mass is scored against the appearance of the phenotype. In this way, traits dependent on multiple genes can rapidly be mapped to the one or more chromosomes upon which the relevant genes reside. This technology offers a powerful new technique to assist the rapid selection of superior plants in traditional plant breeding programmes. Such mapping can also be used in conjunction with molecular cloning procedures to clone the various genes of interest.

In animal breeding also, new technologies have brought about significant advances. Hormone administration to increase ovum production, followed by artificial insemination, can provide up to a dozen or so embryos which can be implanted into surrogate mothers. In a more recent development, ten or more cells may be taken from each fertilized egg before

cell differentiation, and the nuclei of these implanted into unfertilized eggs from which the nuclei have been removed. Each embryo is implanted into a surrogate mother to produce identical offspring. Thus, in theory, several hundred offspring can result from a single mating, considerably reducing the time necessary to introduce a new strain. However, even these more recent developments are limited by the inherent genetic endowment of each species and by the lack of specific methods of elucidating the structure and function of individual genes.

New methods based on molecular biology have aroused considerable interest because they offer the prospect of introducing more rapid and precisely targeted genetic changes than can be introduced through breeding and selection; they are not bound by the genetic diversity of the parent organisms or their sexual compatibility.

These new methods have been made possible by a number of major discoveries made over the past half-century which have built on the pioneering work of Darwin and Pasteur. They include: the demonstration that DNA is the bearer of genetic information; solution of the structure of DNA; and Cohen and Boyer's demonstration, in 1973, that DNA could be constructed in vitro, inserted and expressed in a living organism. These new methods of genetically modifying an organism involve the introduction of novel genetic material in the form of a DNA construct made up in vitro. The novel DNA may be introduced into the host organism as a plasmid or it may be introduced with the intention of integration into the chromosome. Introduction can be by a number of techniques, including: sexual crossing, protoplast fusion or the use of direct gene transfer.

To be of any practical value, the novel DNA introduced into the cells of the host organism must be genetically stable and properly expressed. Expression of the gene products, if achieved, will reflect precisely the nature of the modification made although the effects of the gene product(s) on the metabolism of the organism may not be easy to predict, particularly if the foreign gene comes from an unrelated species.

8. CONCLUSIONS AND RECOMMENDATIONS.

In its consideration of the food safety implications of the application of biotechnology to food production and processing, the Consultation reviewed the past, present and possible future applications of the technology. It examined the scientific principles that would need to be taken into account in assessing the safety of foods (including food ingredients, additives and processing aids) from microbial, plant and animal sources. The conclusions and recommendations of the Consultation are as follows:

Conclusions

a) Biotechnology has a long history of use in food production and processing. It represents a continuum embracing traditional breeding techniques and the latest techniques based on molecular biology. The newer biotechnological techniques, in particular, have very great potential for rapidly improving the quantity and quality of food available. The use of these technologies does not lead to food which is inherently less safe than food from conventional technologies.

b) A number of food additives already exist which are derived from genetically modified micro-organisms. Food products from genetically modified plants under development are likely to be marketed in the near future. Although genetically modified fish and invertebrates could be available in the market-place relatively soon, genetically modified mammals are less likely in the near future.

c) Biotechnological techniques can be used to prepare new, safer and more effective veterinary drugs, bio-pesticides, rhizobia and other products for use in agriculture. Such techniques may also enable agriculture to become an even more important source of industrial chemicals. By enabling the development of highly specific reagents, biotechnology has also led to improved methods of food analysis.

d) Whenever the process by which a food is made is changed, or a new process is introduced, the implications for the safety of the product should be examined. The examination should take into account how the product was obtained, as is necessary for all foods. The extent of the evaluation will depend on the nature of the perceived concerns.

e) The evaluation of a new food will encompass safety and nutritional value. It should use conventional, analogous, food products as a standard, and will need to take into account any processing that the food will undergo as well as the intended use of the food.

f) Comparative data on the closest conventional counterpart are critically important to facilitate the evaluation of a new food, including data on chemical composition and nutritional value. The Consultation believes that such data are not widely available at the present time.

g) A new, multi-disciplinary approach to the safety evaluation of new foods is desirable, based on an understanding of the mechanisms underlying changes in composition. Detailed knowledge of the chemical composition of the food, together with information on the genetic make-up of the organism(s) involved should form the basis of the evaluation and will indicate the necessity for a more traditional approach involving animal testing. The approach will be facilitated by the integration of molecular biology into the evaluation process.

h) The Consultation was able to agree on a set of scientific principles to be applied to the evaluation of the safety of foods produced by

biotechnology although at the present time this would need to be applied on a case by case basis.

- i) In due course it will be possible to develop a framework for the evaluation of all new foods, including those produced by biotechnology. The framework will need to be flexible, with data needs depending upon the nature and use of the product. At the present time there is little experience from which to develop generic criteria for such a framework, and until such time as these criteria can be developed, a case-by-case approach is required.
- j) As far as the products of the newer biotechnologies are concerned, detailed knowledge of their molecular biological properties will facilitate the evaluation process and it is already possible to identify many of the categories of data that will be necessary. In due course it will be possible to identify, on a generic basis, those genetic elements that are likely to be acceptable for use in food-producing organisms.
- k) To facilitate the safety evaluation of foods derived from biotechnology, action at the international level will be necessary to provide timely expert advice in this matter to Member States of FAO/WHO, the Codex Alimentarius Commission, JECFA and JMPR.
- l) The Consultation concluded that because of the rapidity of technological advances in this area, further Consultations on the safety implications of the application of biotechnology to food production and processing would be necessary in the near future.

Recommendations

- a) Comprehensive, well-enforced food regulations are important to protect consumer health and all national governments should ensure that these keep pace with developing technology.
- b) National regulatory agencies should adopt the strategies identified in this report for evaluating the safety of foods derived from biotechnology.
- c) To facilitate the evaluation of foods produced by biotechnology, databases should be established concerning:
 - the nutrient and toxicant content of foods;
 - the molecular analysis of organisms used in food production; and
 - the molecular, nutritional and toxicant content of genetically modified organisms intended for use in food production.
- d) Consumers should be provided with sound, scientifically based information which explains the application of biotechnology in food production and processing and clarifies the safety issues.

e) FAO/WHO, in cooperation with the other international organizations, should take the initiative to ensure a harmonized approach to the safety assessment, by national governments, of foods produced by biotechnology.

f) The Directors-General of FAO and WHO are requested to provide the necessary technical and financial support for timely expert advice on the impact of biotechnology on the safety assessment of foods to Member States of FAO/WHO, the Codex Alimentarius Commission (CAC), the Joint Expert Committee on Food Additives (JECFA) and the Joint Meeting on Pesticide Residues (JMPR).

g) FAO/WHO should establish further consultations in a timely manner, to reconsider the Consultation's advice in the light of scientific and technical advances.

ANNEX 1:

List of Participants:

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Annex 2: Objectives and Terms of Reference of the Consultation.

OBJECTIVES

The Consultation should examine the impact of the biotechnologies on food production and processing, analyse the implications of the use of biotechnologies for food safety, and identify real or potential safety concerns and issues specific to the application of the biotechnologies.

The Consultation should recommend appropriate safety assessment strategies and procedures.

TERMS OF REFERENCE

The Consultation is expected to cover the following:

1. Conduct a review of current and projected products and applications of biotechnology in the area of: (1) Foods, (2) Food Additives, (3) Processing Aids, and (4) Biological Pest Control Agents.
2. Review the technology and identify possible hazards resulting from the application of each of specified biotechnologies.
3. Review current safety-assessment strategies and procedures for these hazard(s) on a product class-by-class basis, and consider alternative approaches where appropriate.
4. Make recommendations to the relevant bodies on how existing safety assessment procedures might be used or modified, or new safety assessment procedures or strategies applied to foods or food products produced by biotechnology.

Annex 3: Definitions Used by the Consultation.

Biotechnology is the integration of natural sciences and engineering sciences in order to achieve the application of organisms, cells, parts thereof and molecular analogues for products and services. (European Federation of Biotechnology, as endorsed by the Joint IUFOST/IUNS Committee on Food, Nutrition and Biotechnology, 1989).

Food Additives means any substance not normally consumed as a food by itself and not normally used as a typical ingredient of food, whether or not it has nutritive value, the intentional addition of which to a food for a technological (including organoleptic) purpose in the manufacture, processing, preparation, treatment, packaging, transport or holding of such food results, or may be expected to result (directly or indirectly), in it, or its by-products, becoming a component of or otherwise affecting the characteristics of such foods. The term does not include "contaminants" or substances added to food for maintaining or improving nutritional qualities (Codex Alimentarius Commission, Procedural Manual, 6th Edition, FAO and WHO, 1986).

Pesticide means any substance intended for preventing, destroying, attracting, repelling or controlling any pest including unwanted species of plants or animals during the production, storage, transport, distribution and processing of food, agricultural commodities, or animal feeds, or which may be administered to animals for the control of ectoparasites. The term includes substances intended for use as a plant growth regulator, defoliant, desiccant, fruit-thinning agent, or sprouting inhibitor, and substances applied to crops either before or after harvest to protect the commodity from deterioration during storage and transport. The term normally excludes fertilizers, plant and animal nutrients, food additives and animal drugs. (Codex Alimentarius Commission, Procedural Manual, 6th Edition, FAO and WHO, 1986).

Food means any substance, whether processed, semi-processed or raw, which is intended for human consumption, and includes drink, chewing gum and any substance which has been used in the manufacture, preparation or treatment of "food" but does not include cosmetics or tobacco or substances used only as drugs. (Codex Alimentarius Commission, Procedural Manual, 6th Edition, FAO and WHO, 1986).

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