International Comparison of Regulatory Frameworks for Food Products of Biotechnology

Prepared for

The Canadian Biotechnology Advisory Committee Project Steering Committee
on the Regulation of Genetically Modified Foods

By

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1 Executive Summary

As part of its work plan for 2000, the Canadian Biotechnology Advisory Committee (CBAC) has undertaken a special project to examine the regulation of foods produced through biotechnology in Canada. This document provides a comparison of the regulatory frameworks in Argentina, Australia, Japan, the United Kingdom and the United States. The objective is to situate Canada internationally with respect to the regulation of agricultural biotechnology products and highlight best practices in a manner that will help CBAC identify issues related to the governance and organization of Canada's regulatory system.

In addition to providing a brief description of the respective regulatory systems, an analysis was conducted using a number of criteria including: legislative basis and public accountability; philosophical approach and regulatory triggers; transparency of the policy making and regulatory decision making processes; approaches to risk assessment; independence of the risk assessment and risk management processes; and the role of post market surveillance.

Some countries have taken divergent approaches to regulation, which is best illustrated by comparing the US and the UK (European Union). The US has adopted an optimistic mindset that essentially approaches the evaluation of new products and technologies by questioning "Why not?", whereas, the European approach is more pessimistic, involving trying to predict the unknown and questioning "Why?".

These varying philosophical approaches have given rise to unique regulatory systems that differ significantly in intent (product vs. process), legislative basis (existing vs. technology specific laws), transparency, and location of decision making authority (institutional vs. political). In Canada and US, scientific risk assessment largely "determines" the regulatory decision, while in the EU, other factors play a crucial role in a decision making process that is "informed" by risk assessment.

Notwithstanding these ideological and political differences, the risk factors considered during an environmental or food safety evaluation are, respectively, the same for each of the countries examined in this comparison. For novel foods, safety assessments have generally been built on the principle that these foods are comparable to existing foods with a history of safe use and that the risk factors (*e.g.*, levels of nutrients and their bioavailability, antinutrients, toxins, and potential for allergenicity) are the same for all foods, regardless of the technology used to produce them. Risk assessments have focused on the defined differences between the novel food and its traditional counterpart, and the effect these differences have on composition, nutritional quality, toxicology, and potential allergenicity. Although not always reflected in the regulatory decision making process, the time to approval, or the ultimate decision to

allow marketing, the scientific opinion on the safety of the products commercialized to date is consistent.

Canada has a robust and scientifically sound system for regulating agricultural products of biotechnology. The existing system has been effective in ensuring that the application of these products in agriculture and food production has not resulted in additional negative environmental consequences or any additional adverse effects on livestock or human health. Canada's regulatory system has been a model for some, and its regulation of products based solely on their intrinsic novelty rather than the technology used to produce them, has remained truest to the scientific principle that biotechnology is not inherently risky.

Internationally, other best practices that were identified include: public notification and a period of public comment in advance of product approval decisions; evidence-based approaches to risk assessment that do not consider social or ethical issues; and the performance of risk assessments by qualified government scientists, supplemented by issue-specific expert panel consultations.

The twin issues of transparency and public participation are significant for Canada and have given rise to legitimate criticisms of the regulatory decision making process. The first is that there is a lack of adequate disclosure of third party information particularly as it relates to the human health and environmental safety testing of new biotechnology products. Regulators have often cited current legal limitations as "an impediment to more closely linking federal research and monitoring capacity with the regulatory functions"[1] and as reasons for not publicly disclosing product-testing data. Second, unlike comparable systems in countries like Australia and the US, Canada's regulatory regime generally makes no provision for public input or comment throughout the risk assessment process leading to a regulatory decision. Policy options to address each of these concerns are feasible and deserve further investigation.

[1] Government response to the report of the House of Commons Standing Committee on the Environment and Sustainable Development, *Pesticides: Making the right choice for the protection of health and the environment*. Pp. 18.

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2 List of Abbreviations

ACGM	Advisory Committee on Genetic Modification (UK)
ACRE	Advisory Committee on Releases to the Environment (UK)
ANZFA	Australia New Zealand Food Authority
ANZFSC	Australia New Zealand Food Standards Council
APHIS	Animal and Plant Health Inspection Service (USDA)
AQIS	Australian Quarantine and Inspection Service
CEPA	Canadian Environmental Protection Act
CONABIA	National Advisory Committee on Agricultural Biosafety (Argentina)
DETR	Department of Environment, Transport and the Regions (UK)
DNA	deoxyribonucleic acid
rDNA	recombinant DNA
EPA	Environmental Protection Agency (US)
EUP	Environmental Use Permit (US EPA)
FDA	Food and Drug Administration (US)
FFDCA	Federal Food, Drug, and Cosmetic Act (US)
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act (US)
FONSI	Finding of No Significant Impact (USDA)
GE	genetically engineered
GMAC	Genetic Manipulation Advisory Committee (Australia)
GMO	genetically modified organism (plural GMOs)
HSE	Health and Safety Executive (UK)
IBC	Institutional Biosafety Committee
IOGTR	Interim Office of the Gene Technology Regulator (Australia)
NIH	National Institutes of Health (US)
NOHSC	National Occupational Health and Safety Commission (Australia)
NRA	National Registration Authority (Australia)
OECD	Organization for Economic Cooperation and Development
SAGPyA	Secretary of Agriculture, Livestock, Fisheries and Food (Argentina)
SENASA	National Service of Health and Quality Agrifood (Argentina)
TGA	Therapeutic Goods Administration (Australia)
TSCA	Toxic Substances Control Act (US)
UK	United Kingdom
US	United States
USDA	US Department of Agriculture

3 Glossary of Terms

Many terms, such as genetically modified (GM) foods, have different meanings depending on context or jurisdiction. As an aid to the reader, we have explicitly defined the meanings of the following terms, as they will be used throughout this document.

Genetic Engineering: A technique whereby individual genes can be copied and transferred to another living organism to alter its genetic make up and thus incorporate or delete specific characteristics into or from the organism. The technology is also referred to as gene splicing, recombinant DNA (rDNA) technology, or genetic modification.

Genetically Modified Food (GM Food): A food, or food ingredient, derived from a plant or animal, including fish, produced through the process of genetic engineering. In this document, the term GE food will be used interchangeably and will mean the same.

Genetically Modified Organism (GMO): Any organism whose characteristics have been intentionally modified through the process of genetic engineering.

Novel Food: The following definition was published in Canada Gazette Part I on September 26, 1998, and will be used throughout this document:

A. A substance, including a microorganism, that does not have a history of safe use as a food;
B. A food that has been manufactured, prepared, preserved or packaged by a process that:
   i. has not been previously applied to that food, and;
   ii. causes the food to undergo a major change.
   "Major change" means, in respect of a food, a change in the food that, based on the manufacturer's experience or generally accepted theory, may have an adverse affect on:
      a. the composition, structure or nutritional value of the food or its generally recognized physiological effects;
      b. the manner in which the food is metabolized in the body, or;
      c. the microbiological safety, the chemical safety or the safe use of the food.
C. A food that is derived from a plant, animal or microorganism that has been genetically modified such that:
   i. the plant, animal or microorganism exhibits characteristics that were not previously observed in that plant, animal or microorganism;
   ii. the plant, animal or microorganism no longer exhibits characteristics that were previously observed in that plant, animal or microorganism, or;
   iii. one or more characteristics of the plant, animal or microorganism no longer fall within the anticipated range for that plant, animal or microorganism.

Plant with Novel Trait (PNT): A plant variety/genotype possessing characteristics that demonstrate neither familiarity nor substantial equivalence to those present in a distinct, stable population of a cultivated species of seed in Canada and that have been intentionally selected, created or introduced into a population of that species through a specific genetic change.

4 Introduction

4.1 Preamble

The Canadian Biotechnology Advisory Committee (CBAC) is an independent expert advisory committee established in September 1999 by the federal government. Its mandate is to provide advice to the Biotechnology Ministerial Coordinating Committee on broad policy issues associated with the ethical, social, regulatory, economic, scientific, environmental and health aspects of biotechnology.

The first novel food approved in Canada in 1994 was an imidazolinone herbicide tolerant corn selected by tissue culturing somatic embryos on imidazolinone containing media (Health Canada 1994). Since that time, Canada has approved a total of 43 novel food products, many of which have been produced through genetic engineering. A key factor in determining the acceptance of these products has been the confidence of Canadians in the federal government's regulatory system for biotechnology products. The past year has seen a significant increase in the activities of action groups, in both Canada and abroad, to mobilize public opinion against the adequacy of current government approaches to ensuring the safety of novel foods.

As part of its work plan for 2000, CBAC has undertaken a special project to examine the regulation of novel foods in Canada (CBAC 2000). In support of that activity, this document provides an international comparison of the regulatory regimes in Argentina, Australia, Japan, the United Kingdom (UK) and the United States (US). The objective of this analysis is to situate Canada internationally with respect to the regulation of agricultural biotechnology products and highlight best practices in a manner that will help CBAC identify issues related to the governance and organization of Canada's regulatory system.

4.2 Document Structure

This comparison has been organized to provide a broad overview of the agricultural biotechnology regulatory framework in each country followed by a more detailed functional analysis of the key guidelines and/or regulations governing scientific innovation, environmental release of genetically modified organisms, and food safety assessments of genetically engineered and other novel foods.

A number of key comparators were developed as an aid to analyzing the different regulatory systems. These were: legislative basis and public accountability; philosophical approach and regulatory triggers; transparency of the policy making and regulatory decision making processes; approaches to risk assessment; independence of the risk assessment and risk management processes; and the role of post-market surveillance. The regulatory systems of each country were assessed according to these criteria and presented in a summary comparison.

Finally, specific processes or attributes of particular regulatory systems that we believe represent best practices in the regulation of agricultural biotechnology products were identified.

5 Description of Regulatory Frameworks

This section presents an overview of the agricultural biotechnology regulatory systems of Argentina, Australia, Japan, the UK, and the US. The purpose is to highlight the specific guidelines, regulations, and procedures that govern laboratory experimentation with genetically modified organisms (GMOs), experimental field trials and unconfined general environmental release of GMOs, and the safety assessment of genetically engineered (GE) and other novel foods.

All of the information for this analysis was obtained from publicly available sources provided by the respective regulatory authorities in each country, and from personal communications with selected regulatory officials.

5.1 Argentina

5.1.1 Overview

Argentina regulates biotechnology, including transgenic plants and genetically engineered food products, through a combination of GMO-specific legislation and preexisting laws covering seeds and veterinary products (Flint *et al*. 2000). Approving the environmental release of GMOs, and their use in human food or livestock feeds, is the responsibility of the Secretary of Agriculture, Livestock, Fisheries and Food (SAGPyA), under regulations administered by SENASA (National Service of Health and Quality Agrifood) (Table 1). The regulation of therapeutic products obtained from biotechnology is the responsibility of the Ministry of Health.

In 1991, SAGPyA created the Comision Nacional Asesora de Biotecnologia Agropecuaria (The National Advisory Committee on Agricultural Biosafety; CONABIA) as a mechanism to provide advice on the technical and biosafety requirements to be met in environmental releases, human food, and livestock feed uses of genetically engineered plant and animal materials (CONABIA 2000). CONABIA's membership is composed of both public and private sector representatives with a wide range of expertise in agricultural biotechnology. Members are selected according to a transparent process (SAGyPA Disposition N° 004/00) and are approved by the Secretary of Agriculture, Livestock, Fisheries and Food. In addition to technical coordination by SAGPyA, the committee composition is as follows:

- Public Sector
  INASE: National Institute of Seeds
  SENASA: National Service of Health and Quality Agri-Food

INTA: National Institute of Agricultural Technology
CONICET: National Council of Technical and Scientific Research
University of Buenos Aires
Secretary of Sustainable Development and Environmental Policy
Ministry of Health

- Private Sector
  - Argentine Association of Seed Producers
  - Argentine Forum on Biotechnology
  - Argentine Society for Ecology
  - Argentine Chamber of Agrochemicals
  - Argentine Chamber of Veterinary Products

Table 1: Argentine regulatory authorities for biotechnology.

Authority	Jurisdiction	Laws and Regulations
Secretary of Agriculture, Livestock, Fisheries and Food	Creation of CONABIA	Resolutions SAGyP N° 124/91, N° 669/93, and N° 328/97.
SENASA (National Service of Health and Quality Agrifood)	Environmental release of transgenic materials and assessment by CONABIA	Resolutions SAGyP N° 656/92, N° 837/93, and N° 289/97.
	Safety assessment of genetically engineered foods and food ingredients	Resolution SAGyP N° 511/98.
	Plant protection and agricultural production	Decree-Law N° 6704/66.
	Seeds registration	Decree-Law N° 20.247/73.
	Veterinary products	Decree-Law N° 13.636/49.

The regulatory framework for biotechnology encompasses the contained use, deliberate release (*i.e.*, confined field trials) and commercialization of GMOs. Under this framework, specific regulations were developed to establish conditions under which environmental releases of transgenic materials may be conducted and the resulting data reviewed by CONABIA (Resolutions SAGyP N° 656/92, N° 837/93, and N° 289/97). Additional regulations, administered by SENASA, apply to safety evaluations of foods and food ingredients containing or composed of GMOs (SAGPyA N° 511/98). As well, all products must comply with existing regulations related to plant protection (Decree-Law of Agricultural Production Health Defense N° 6704/66 and its amendments), seeds registration (Seed and Phytogenetic Creations Law N° 20.247/73), and animal health (Law of Veterinarian Products Supervision of Their Elaboration and Creation N° 13.636/49).

Argentine regulations concerning the environmental release of GMOs were developed by CONABIA and are enforced by the Secretary of Agriculture, Fisheries and Food. Similarly, for feed and food evaluation, the standards are defined by SENASA and the Secretary is responsible for their enforcement. In practical terms, Argentina's regulations are almost completely directed towards those products obtained by genetic engineering. Nevertheless, the philosophy of the regulation is based on the properties of the new trait and not on the process used to obtain it. All products are regulated, however, those obtained by conventional methods are regulated very lightly, while those obtained by genetic engineering are subjected to very rigorous oversight.

In addition to the scientific assessment of risk performed by CONABIA and SENASA, all products are subject to an economic analysis by the National Office of Agrifood Markets within SAGPyA, which studies the potential impact of the approval on domestic and international markets. This step is one means by which non-scientific concerns may be addressed. Changes to regulations and/or policy related to agricultural biotechnology are published in the *Official Bulletin*.

Fig. 1. Product movement through the Argentine regulatory system

Pre-market notification is mandatory for biotechnology products, and in the case of genetically engineered crops, the procedure involves three steps, as follows:

1. Once a permit for introduction into the environment is granted and biosafety is adequately established, an application for extensive cultivation, called flexibilization, can be submitted. Granting this status means that for future releases only information on: sown area; date of seeding; site of release; and harvest date is required.

2. In order to obtain a commercialization permit, the GE crop must meet all the requirements under regulations administered by SENASA for human use and animal consumption.

3. In addition to approval for food and feed uses, a technical report by the National Office of Agrifood Markets is required to assess the impact of the product on Argentine exports.

The final decision is the responsibility of the Secretary of Agriculture, Livestock, Fisheries and Food, and is based on the results of these three steps. Additionally, GE animals, microorganisms and/or their products are subject to environmental and food safety assessments prior to marketing.

5.1.2 Innovation and Scientific Discovery

Research involving genetic manipulation is subject to specific guidelines that define conditions of confinement and related safety procedures. These guidelines are similar in purpose and content to other internationally recognized standards, such as the Medical Research Council of Canada "*Guidelines for the Handling of Recombinant DNA Molecules and Animal Viruses and Cells*". When the research involves a release to greenhouses or to the open field, regulations recommended by CONABIA are applied for agricultural species.

5.1.3 Environmental Release

The environmental release of GMOs is controlled at three levels through the issuance of licenses for experimentation in greenhouses, field trials and pre-commercial multiplication, and permits for flexibilized conditions for large-scale releases.

Risk assessments and subsequent monitoring of experimental field trials are the responsibility of the SAGPyA. The following issues are considered during the risk assessment: the biological characteristics of the GMO; the features of the agro-ecosystem where the trial is to be carried out; the necessary conditions of reproductive isolation and post harvest land use; and the technical capacity of the

applicant. Risk assessments are performed on a case-by-case basis; each case represents a specific transformation event, applicant organization, and scale of release.

Compliance with the conditions of authorization is monitored through site inspections (at flowering and at harvest) by the National Institute of Seeds and SENASA. CONABIA publishes an Annual Report, which provides information for each confined trial and describes the plant crop, the introduced trait, and the petitioner (CONABIA 1999). The Annual Report also reviews the applications that have been received for flexibilization and any changes to policy or regulations.

In its evaluation of applications for extensive cultivation (*i.e.*, flexibilization), CONABIA considers the following environmental risk factors:

- Capacity of the GMO to survive, establish and disseminate (which effectively means a plant's tendency to weediness);
- Potential for horizontal gene transfer or gene exchange with other organisms;
- Products of expression of introduced sequences;
- Phenotypic and genotypic stability;
- Pathogenicity to other organisms;
- Potential to produce environmental toxins; and
- Potential harmful effects on humans.

Among the possible risks to the environment, the impact on the agro-ecosystem is also considered with respect to possible changes in agricultural practices.

Following commercialization, there are mechanisms to follow up on any predictable consequences of environmental introduction, such as the potential for selecting resistant insect populations arising through the adoption of *Bt*-crops. Analogous to the situation in Canada and the US, an industry developed and implemented insect resistance management plan has been approved, with modification, by CONABIA. Grower compliance is addressed through a detailed communications strategy and a non-binding acknowledgement document.

5.1.4 Food Safety

Prior to marketing, all genetically engineered organisms, or products derived from them, that are intended for human food or livestock feed use are subject to a risk assessment by SENASA. Safety data supplied by the applicant are reviewed to ensure that the following issues have been adequately addressed:

- Presence of natural toxicants;
- Toxicity of the transgenically expressed protein;

- Amino acid sequence homology between transgenically expressed protein(s) and known allergens;
- Nutritional modifications, with a focus on any changes due to the genetic transformation;
- Changes in bioavailability of macro- and micro-nutrients; and
- Characterization of the modified food regarding suitability for human and animal consumption.

5.1.5 Post-Marketing Considerations

Under Resolution Nº 511/98, which is currently under review, companies with products approved for commercialization "are not exempted" from a standard of care regarding continued surveillance for unanticipated effects. Such "new information" must be reported to SENASA for evaluation, which could affect the commercialization decision. The revised Resolution may incorporate explicit mandatory requirements for post-market surveillance, but this issue remains a matter of much discussion (C. Vicien, personal communication).

At present, the segregation of genetically engineered commodities within the food supply chain is not practiced to any significant extent, nor is it seen as practicable with the current infrastructure. Should segregation become an issue, it will have an obvious impact on Argentina's labelling requirements for genetically engineered foods, which are currently similar to those of Canada and the US. Bioengineered foods in which the nutritional quality, toxicology, or potential for allergenicity is significantly altered must be so labelled. There are no organized programs of population health surveillance related to any particular kind of food, including genetically engineered foods.

5.2 Australia

5.2.1 Overview

In Australia, the regulation of biotechnology and its products is coordinated under five different systems (IOGTR 1999) by the Australia New Zealand Food Authority (ANZFA), the Therapeutic Goods Administration (TGA), the National Registration Authority (NRA), the National Occupational Health and Safety Commission (NOHSC), and the Australian Quarantine and Inspection Service (AQIS) (Table 2). The Environment Risk Management Authority is responsible for regulating the environmental release of GMOs in New Zealand.

Table 2: Australian regulatory authorities for biotechnology.

Agency	Jurisdiction	Laws/Regulations
ANZFA	Food standards, including GE foods, for all of Australia and New Zealand. Recommendations approved by ANZFSC	Australia New Zealand Food Authority Act 1991; Standard A18 - Food Produced Using Gene Technology
TGA (which contains the IOGTR)	Import, manufacture, and supply of all therapeutic products. Within the IOGTR, GMAC conducts environmental safety assessments of GMOs.	Therapeutic Goods Act 1989; proposed new legislation called Gene Technology Bill 2000.
NRA	Agricultural and veterinary chemicals, including plant-pesticides (*e.g.*, peticidal plants).	Agricultural and Veterinary Chemicals Code Act 1994
NOHSC	Industrial chemicals.	National Industrial Chemicals Notification and Assessment Scheme
AQIS	Imports and exports of agricultural commodities, including GE plants.	Export Control Act 1982.

The Genetic Manipulation Advisory Committee (GMAC), which is housed within the Interim Office of the Gene Technology Regulator (IOGTR) of the TGA, is a non-statutory body responsible for overseeing the research, development and use of novel genetic manipulation techniques in Australia, and the environmental release of GMOs. GMAC is concerned with any operation that results in or uses organisms of novel genotype produced by genetic manipulation that fall under its scope of review (GMAC 1999a). GMAC has defined its scope as: *"any experiment involving the construction and or propagation of viroids, viruses, cells or organisms of novel genotype produced by genetic manipulation which are either unlikely to occur in nature, or likely to pose a hazard to public health or to the environment"*.

The Committee is made up of approximately 20 part-time members appointed by the Minister for Health and Aged Care. The membership of GMAC includes a wide range of expertise in fields that are relevant to risk assessment of genetic manipulation work. This includes experts in the fields of molecular biology, ecology, plant genetics, microbial genetics, animal genetics, virology, entomology and biosafety engineering.

Anyone wishing to release a GMO into the environment, either in the course of an experimental field trial or as a general (*i.e.*, commercial) release, must submit a proposal to GMAC. In the process of considering an application and conducting their risk assessment, GMAC engages in two rounds of public consultation – the first round seeks public comments on the application and the second round seeks comment on the Committee's proposed decision. In both cases, public notification is provided by advertisements in regional and national newspapers, via the Internet, by direct mail to all persons who have registered an interest in receiving such information, and in the *Commonwealth of Australia Government Notices Gazette*.

The need for a new system of regulation to replace the existing voluntary scheme as administered through GMAC arose from a number of considerations, which included that:

- the voluntary system of compliance with GMAC guidelines was not designed to provide for product regulatory approvals, as its original focus was the oversight of research;

- the existing product regulatory system was not designed with GMOs in mind and as a result there were gaps and deficiencies within the framework; and

- public confidence in gene technology would be enhanced by ensuring that development and applications were accompanied by appropriate risk assessment and controls.

Through the proposed Gene Technology Bill 2000 (IOGTR 2000), steps are being taken to create a regulatory body that will subsume the functions of GMAC. Until then, compliance with GMAC guidelines is on a voluntary basis. The new legislation will establish a statutory officer, the Gene Technology Regulator (GTR), for the purposes of performing functions under the Bill, and three key committees (the Gene Technology Technical Advisory Committee, the Gene Technology Ethics Committee, and the Gene Technology Community Consultative Group) to provide scientific, ethical and policy advice.

This new legislation will regulate, for the first time, all "dealings" (*e.g.*, research, manufacture, production, commercial release, and import) with live, viable organisms that have been modified by techniques of gene technology, including the progeny of such GMOs that also share a genetically modified trait. Examples include the production of crops and animals that have been genetically engineered, and laboratory research involving the genetic modification of animals, plants, bacteria, and viruses. Products that are currently subject to national regulation by existing agencies such as the TGA (therapeutic products) and ANZFA (processed food products) will not be regulated by the GTR.

Under the Australian Constitution, the responsibility for regulating the safety of food produced for consumption within Australia is vested in the States and Territories. Australia therefore, has a complex and varied food regulatory system, covering several agencies and types of legislation spread across three levels of government. A 1998 review of food regulation found about 150 Acts and associated regulations related to food or agri-food businesses in Australia, which were administered by several Commonwealth agencies, over 40 State and Territory agencies, and over 700 local governments.

National food standards are developed by ANZFA and are adopted by the States and Territories by reference and without amendment after being agreed by a majority of members of the Australia New Zealand Food Standards Council (ANZFSC), which is

comprised of Commonwealth, State, Territory and New Zealand health ministers. In July 1998, ANZFA established *Standard A18-Food Produced Using Gene Technology*, which came into force on May 13, 1999 (ANZFA 1999a, 1999b). Under this Standard, the sale of food produced using gene technology is prohibited unless the food is included in the Table to clause 2 of the Standard. The Standard requires that a pre-market safety assessment be conducted on all foods produced using gene technology. However, the Standard provides an exemption for those foods currently on the market provided that an application was accepted by ANZFA on or before April 30, 1999, that the food is lawfully permitted in a country other than Australia or New Zealand, and that ANZFSC has not become aware of evidence that the food poses a significant risk to public health and safety.

ANZFA prepares a detailed safety assessment report that is made available to the community and other stakeholders through consultations that form part of the approval process. Through these consultations, the views of the public are sought and legitimate issues must be addressed before a final decision is made by the ANZFSC on the approval of the GE food.

To date, ANZFA has completed food safety assessment and recommended approval of glyphosate tolerant soybeans and *Bt* cotton. Assessments for 17 other GM crops, the majority of which have been modified to be herbicide tolerant and/or to resist insect pests, are currently underway and are due to be completed by mid to late 2000.

5.2.2 Innovation and Scientific Discovery

GMAC has published non-statutory *"Guidelines for Small Scale Genetic Manipulation Work"* (GMAC 1998a) which specify the procedures to be followed by institutions and researchers intending to undertake genetic manipulation work, and detail the requirements for containment facilities. Any institution that conducts genetic manipulation work is required to set up an Institutional Biosafety Committee (IBC) to supervise work and facilities. GMAC monitors the operations of IBCs and provides them with advice about potential hazards. Proposals for genetic manipulation work are assessed by GMAC on a case-by-case basis.

In New Zealand, the Advisory Committee on Novel Genetic Techniques (ACNGT) fulfils a similar role to that of GMAC.

5.2.3 Environmental Release

The responsibility of GMAC to oversee GMO research in Australia extends to examining and providing advice on the deliberate environmental release of GMOs either in experimental field trials or as commercial plantings (Table 3). A "field trial" is defined in GMAC's *"Guidelines for the Deliberate Release of Genetically Manipulated*

Organisms" (GMAC 1998b) as: "a *deliberate release of a genetically manipulated organism in the open environment on a restricted scale, for a limited period, and under conditions which minimise or reduce the potential for dissemination or persistence of the organism or its genetic material into the environment*" (*i.e.*, reproductive isolation). General releases, or commercial plantings, are distinguished from field trials in that they do not have provisions of reproductive isolation. However, GMAC reserves the right to place conditions or restrictions on the conduct of general release proposals.

Table 3: Key steps in the decision making process for deliberate release of a GMO into the environment.

Receipt of Application	**IOGTR:** - notifies the Commonwealth Health Minister of receipt; - prepares newspaper advertisements to notify the public; and - prepares a summary of the application and a relevant Fact Sheet.
Call for input into the assessment of the application	**The Commonwealth Health Minister:** - notifies the Prime Minister, the Environment Minister and other Ministers of receit of the application; and - writes to the State Premiers and Territory Chief Ministers seeking input into the assessment. **IOGTR:** - places advertisement in newspapers advising of the availability of (1) summary information, (2) the Fact Sheet, (3) the full application; - forwards the application to GMAC to begin the scientific assessment; - forwards the application to Environment Australia, (EA) for the environmental risk assessment to begin; and - begins a literature review.
Application is subjected to a risk assessment	- IOGTR completes literature review; - EA completes an environmental risk analysis; - GMAC meets to consider risk assessment including environmental risk analysis, literature review results and public comments; and - GMAC provides advice to the IOGTR.
Decision is made	- IOGTR considers GMAC's advice and makes recommendation to Health Minister; - Health Minister consults with relevant Ministers; - Decision on proposal is made by Health Minister.
Decision is notified	- IOGTR informs applicant of decision; - IOGTR provides written response to submissions; and - IOGTR prepares and releases Public Information Sheet summarizing the risk assessment and decision. - If approved, Commonwealth enters into legally binding agreement with applicant.

The *"Guidelines for the Deliberate Release of Genetically Manipulated Organisms"* (April 1998) specify the information requirements pertaining to proposed environmental releases of all GMOs (plants, animals, microorganisms). These requirements include information on:

- the species to be released, including possible pathogenicity and origin of inserted DNA;
- habitat and ecology of the parent organism, the occurrence of known predators or parasites of the organism, any known interactions between the

GMO and its parent organism in the environment, and other anticipated direct or indirect ecological effects;

- complete molecular characterization of the GMO including method used in its production;
- stability, survival and gene transfer (outcrossing) including an assessment of possible competitive advantage of the GMO over its unmodified parent;

When GMAC receives a proposal for a deliberate release of a GMO into the environment, it: a) publishes a notice of the proposed release in the *Commonwealth of Australia Government Notices Gazette* as well as national and regional newspapers; b) circulates a description of the application to interested individuals and organizations who have registered with GMAC for this purpose; and c) sends the description to the local council for the area of the release and to relevant State and Commonwealth bodies (Fig. 2).

Fig. 2. Sample notification of an application for a small scale confined field trial

Organisations Proposing Release:
Queensland Dept. of Primary Industries
GPO Box 46
Brisbane, QLD 4001

Organism to be released: Pineapple *(Ananas comosus)*

Purpose of the release: The aim of the trial is to assess the commercial utility of pineapples genetically modified to control blackheart. Blackheart is a discolouration of the tissue of the pineapple fruit. In Australia, blackheart occurs in the field in winter-grown crops, causing heavy losses to industries due to downgrading of fruit quality, immature harvest of fruits and reduced winter production. The trial will involve testing of modified pineapple lines for agronomic performance, activity of gene control elements (promoters) and resistance to blackheart.

Brief description of the nature and effect of the genetic modification: The modified pineapple lines contain additional copies of the pineapple polyphenol oxidase (PPO) gene. The addition of extra copies of the PPO gene is intended to reduce expression of the PPO enzyme, which is believed to be responsible for the tissue discolouration in blackheart. The genetically modified pineapple lines also contain selectable marker genes which enable identification and selection of the modified plants in the laboratory.

The trial will also include a study of the activity of different promoters. Promoters are genetic ‚switches™ which, when coupled with a gene of interest, cause that gene to be expressed at high levels in particular tissues of a plant. The pineapple plants to be used in this study contain different promoters linked to marker genes.

Location and size of trial: Up to 735 plants on 0.12 hectares in south-east Queensland.

Further information: The institution's contact officer for this proposal is Dr Michael Smith, telephone (07) 5441 2211, facsimile (07) 5441 2235.

If GMAC considers that the proposed release is likely to have a significant effect on the environment or require the application of specific management plans, it may refer the proposal to government regulatory bodies for consideration. For example, when *Bt* cotton was proposed for general release, GMAC considered the environmental risks that might be associated with the plant. But, since *Bt* cotton also acts as a "plant pesticide", it required approval by the National Registration Authority (NRA) for Agricultural and Veterinary Chemicals before it could be released commercially. GMAC's expert advice on measures to manage the risk of selection of insects with resistance to the *Bt* toxin was provided to the NRA. This formed the basis of the NRA's legally binding requirement for a resistance management strategy as a condition of use and sale of the *Bt* cotton.

After GMAC has advised that a deliberate release may proceed, it will issue a Public Information Sheet (GMAC 2000) to individuals and organizations, including journalists, who have registered with GMAC for this purpose. Copies of the Public Information Sheet will also be forwarded to the members of the public who commented on the initial notification of the release, to the municipal council in the area of the release, and to relevant State and Commonwealth bodies. The Public Information Sheet will contain a description of the organism to be released and the procedures to be undertaken during and after the release, as well as a summary of GMAC's reasons for its decisions on the proposal.

GMAC also publishes an Annual Report (GMAC 1999b) that summarizes the numbers of proposals considered and approved in each category, the types of products being trialed, Committee activities, and a brief synopsis for each proposal considered or approved.

Regulations concerning the environmental release of GMOs in New Zealand are enforced by the Environmental Risk Management Authority under the Hazardous Substances and New Organisms Act.

5.2.4 Food Safety

GE foods are regulated by *Standard A18 – Food Produced Using Gene Technology* in the Australian Food Standards Code. Under Standard A18, these foods are only permitted for sale in Australia and New Zealand if they have been assessed by ANZFA, are considered safe and have been approved by the health ministers of the two national and eight State and Territory governments as members of ANZFSC.

ANZFA's safety assessment process for GE foods is based on the following key principles, which mirror those developed through the expert consultation processes of the OECD and the WHO/FAO:

- safety assessments use scientific, risk-based methods;
- safety assessments are conducted on a case-by-case basis;
- both the intended and unintended effects of the genetic modification are considered; and
- where appropriate, comparisons are made to conventionally produced foods (*e.g.*, concept of substantial equivalence).

In assessing the safety of a GE food, ANZFA requires the proponents to submit a complete data package that, at a minimum, addresses the following issues (ANZFA 1999c):

- **Nature and stability of the genetic modification**: Includes a complete molecular characterization of the genetic modification, including data demonstrating that the novel genetic material has been stably integrated in the host genome and that the phenotype is stably maintained over several generations.

- **General safety issues:** Factors considered include the levels of nutrients, antinutrients, natural toxicants and ability to support typical growth and well being. The nature and amounts of the novel proteins expressed in the GE food are examined to determine if the expressed protein has been modified in any unexpected way. The impact on human health from potential transfer of novel genetic material, including antibiotic resistance genes, to cells, including microorganisms, in the human intestinal tract is also considered.

- **Toxicological issues**: These include a consideration of the levels of naturally occurring toxins as well as the potential toxicity of any novel proteins. The levels of naturally occurring allergenic proteins as well as the potential allergenicity of any novel proteins are also considered.

- **Nutritional issues**: These are usually addressed through an understanding of the genetic modification and its consequences together with an extensive compositional analysis of the food. Ordinarily, ANZFA does not consider animal feeding studies as essential for determining safety, but may require them when the compositional analysis indicates significant differences in a number of important components or nutrients, or where there is a concern that the bioavailability of key nutrients may be compromised by the nature of the genetic change.

The legal requirement of the Australian food standard setting process requires full disclosure and public consultation. In addition, the decisions taken by officials in the administration of legislation are subject to a variety of appeal mechanisms. These processes help ensure that the interests of affected groups are taken into consideration and that provisions are appropriately administered.

All applications for safety determination of GE foods are subject to public notification and comment, and in accordance with the procedures described in Section 17 of the Australia New Zealand Food Authority Act 1991, ANZFA seeks public comment on all proposed amendments (*i.e.*, GE food approvals) to Standard A18 of the Food Standards Code. In the process of soliciting public comment, ANZFA publishes a draft risk analysis report (*cf* ANZFA 2000a) that provides a background to the application, highlights the issues addressed during the risk assessment, summarizes public

comment submitted in response to the notification of application, and deals with legitimate issues raised in public comments.

Based on ANZFA's advice, the final decision on any new submission is made by the ANZFSC, following which, ANZFA publishes the finalized Risk Analysis Report.

5.2.5 Post-Market Considerations

Standard A18 incorporates a mandatory provision for labelling genetically modified foods in circumstances where the nature of the food has been significantly changed with respect to its nutritional quality, composition, allergenicity, or end use. For those foods that must be labelled (*e.g.*, products that are not judged to be substantially equivalent), the label must indicate the biological origin and nature of the characteristic or property modified. Negative claims (*e.g.*, that foods are not, or do not contain, genetically modified material) are permitted, provided they do not contravene existing fair trading laws relating to consumer deception. In response to requests from a number of consumers and consumer groups, ANZFA was asked by ANZFSC in December 1998 to develop an amendment to Standard A18 to extend labelling to all GE foods or ingredients.

On July 28, 2000, ANZFSC agreed to new labelling rules for GE foods (ANZFA 2000b). The new food standard will require the labelling of food and food ingredients where novel DNA and/or novel protein is present in the final food. It also requires labelling of food and ingredients where the food has altered characteristics.

Exempt from these requirements are:

- highly refined food, where the effect of the refining process is to remove novel genetic material and/or novel protein;
- processing aids and food additives, except where novel genetic material and/or novel protein is present in the final food;
- flavours which are present in a concentration less than or equal to 0.1% in the final food; and
- food prepared at point of sale (*e.g.*, restaurants, hotels, takeaways).
- The new standard allows any one ingredient in a food to contain up to 1% of genetically modified material where its presence in the ingredient is unintended.

Australia does not currently conduct any post-market surveillance of the potential adverse or beneficial effects of GE foods. While it is seen by many as a logical follow-up to the initial scientific risk assessment, it is recognized that there are limitations to the application of epidemiological studies, particularly in relation to food components. A key limitation is the lack of any system for monitoring the

consumption patterns of novel foods in the population, and health effects in both "exposed" and "non-exposed" individuals/populations, so that risk estimates can be derived. ANZFA has committed to monitoring international activities in this area (M. Healy, personal communication), including any recommendations arising from the OECD Taskforce on the Safety of Novel Foods and Feeds (OECD 2000a).

5.3 Japan

5.3.1 Overview

Japan's approach to ensuring the safe use and application of recombinant DNA technology has been through a series of voluntary guidelines that are administered by four government agencies (OECD 2000b). These guidelines cover the application of recombinant DNA technology in confined laboratory settings, the industrial application of GMOs and recombinant DNA technology, the environmental release of GMOs, and the safety assessment of genetically engineered foods. The relevant government departments are: Ministry of Science and Technology; Ministry of International Trade and Industry; Ministry of Agriculture, Forestry and Fisheries; and Ministry of Health and Welfare (Table 4). Each Ministry has produced its own set of guidelines, which are similar in structure and closely follow the recommendations of the Organization for Economic Cooperation and Development (OECD).

Table 4: Japanese regulatory authorities for biotechnology.

Ministry	Jurisdiction	Laws/Guidelines
Science and Technology	Genetic manipulation work in contained laboratory facilities.	Guidelines for rDNA Experimentation (except at universities)
International Trade and Industry	Industrial applications of biotechnology and use of GMOs.	Guidelines for the Industrialization of rDNA Technology.
Agriculture, Forestry and Fisheries	Environmental release of GMOs	Guidelines for the Application of rDNA Organisms in Agriculture, Forestry, Fisheries, the Food Industry and Other Related Industries; Guidelines for Safety Assessments of Application of rDNA Organisms in Feed;
Health and Welfare	Foods and food ingredients containing GMOs or produced using recombinant DNA technology.	Guidelines for Foods and Food Additivies Produced Through rDNA Techniques; Article 7, Food Sanitation Law (proposed mandatory notification);

The Ministry of Science and Technology deals only with submissions for genetic manipulation work done at an experimental level in public, private, or university laboratories. The Ministry's "*Guidelines for Recombinant DNA Experiments*", first published in 1987, prescribe containment facilities and laboratory practices for work performed in either a small- (up to 20 litres) or large-scale situations. There is neither a general notification requirement, nor a government review system for the experiments covered by the Guidelines.

For industrial applications of biotechnology, the "person in charge of a working organization" is responsible for the evaluation of the safety of GMOs used in

manufacturing processes. In 1986, the Ministry of International Trade and Industry published voluntary Guidelines as an aid to companies in categorizing GMOs according to levels of risk and establishing Good Industrial Large-Scale Practice.

The Ministry of Agriculture, Forestry and Fisheries is responsible for ensuring the safety of animal feeds and feed additives, and the environmental safety of transgenic plants in confined field trials and commercial agriculture. As an aid to developers in conducting their safety assessments, the Ministry has published guidelines for evaluating the ecological and environmental effects of cultivation and for the application of GMOs in feeds and feed additives. When safety assessments have been completed in accordance with the relevant guidelines, the developer may request the responsible government minister to approve the safety criteria and procedures used to ensure compliance with that guideline.

In 1989, the Department of Health and Welfare established a Sub-Committee on Biotechnology within the National Food Safety Council in order to advise the Minister on technical matters related to foods and food ingredients produced by the application of recombinant DNA techniques. The Sub-Committee's guidelines establish "*Standards for Safety Assessment of Foods and Food Additives Produced by Recombinant DNA Techniques*" (MHW 2000a) and "*Guidelines for Manufacturing Foods and Food Additives Produced by Recombinant DNA Techniques*" (MHW 2000b) which are not legally binding, but are applied by developers on a voluntary basis. The risk assessment process described in these guidelines is based on the concepts of substantial equivalence and familiarity as espoused by the OECD.

While there are no known instances of GE foods being placed on the Japanese market without safety assessment, a revision of the current voluntary scheme has been started with a view to making it mandatory (MHW 2000c). Two of the reasons for moving toward a mandatory system are:

- Increased international trade in GE foods and the coming commercialization of new types of GE foods that have been purposefully developed to be not "substantially equivalent" (*i.e.*, functional foods, nutraceuticals, edible vaccines); and

- The implementation, in April 2001, of mandatory labelling of GE foods by the Ministry of Agriculture, Forestry and Fisheries.

Under Article 7 of the existing Food Sanitation Law, the Minister of Health and Welfare has the authority to establish specifications for food components and standards for manufacturing foods and food additives with a view to preserving and promoting public health. Rather than establish new legislation, the proposed revision will amend

the "Specification and Standards for Foods, Food Additives and Other Related Products" so that "*If a food is made of all or part of an organism obtained by recombinant DNA techniques, or if a food contains all or part of an organism obtained through recombinant DNA techniques, the organism shall undergo food safety assessment by the Minister of Health and Welfare*". The planned revision is expected to increase the transparency of the safety evaluation process and to increase consumer confidence.

From April 2001, the manufacture, sale, and import of GE food products that do not conform to the Standard will be prohibited. Violations of the Standard will be subject to administrative monetary penalties or criminal punishment and non-conforming products subject to recall or return to the exporting country.

5.3.2 Innovation and Scientific Discovery

The Japanese government's "*Guidelines for rDNA Experimentation*" are similar in scope and intent as those published in other countries and have been modelled after the United States National Institutes of Health guidelines. Prior to the commencement of experiments, a safety assessment is performed by the research institution proposing the work, and the physical and biological containment levels are selected based on this assessment. A safety committee, which has to be established at each institution engaged in genetic manipulation work, advises the head of the institution on the acceptability of planned experiments.

The Guidelines stress individual responsibility and the heads of institutions are held accountable for the work undertaken within their institution, for approving or rejecting plans for experiments, and for ensuring adequate training for staff.

The Ministry of Science and Technology has a 15 member advisory committee on recombinant DNA activities. Applications to the committee require one to two months for processing and approval is usually automatic provided the applicant can demonstrate appropriate containment facilities and procedures.

Similar, but separate guidelines have been published by the Ministry of Education to cover recombinant DNA research undertaken at university facilities.

5.3.3 Environmental Release

According to guidelines published by the Ministry of Agriculture, Forestry and Fisheries (MAFF 1995), all genetically engineered plants destined for commercial agriculture must be evaluated in a "simulated model environment" (*i.e.*, confined field trial) prior to submission of the environmental safety assessment for review.

At this stage, the transgenic plant is cultivated under conditions of reproductive isolation in order to investigate its properties as an agricultural product, including weediness and hybridizing potential with related species. The results of field tests are incorporated into the environmental assessment of the potential impact commercial release could have on the agriculture and ecology of Japan.

The requirements for prior evaluation in a simulated model environment apply to the domestic cultivation of transgenic crop plants as well as to imports of such plants that may propagate in the natural environment. This includes the importation for processing of edible oil seeds for which there is a possibility of natural propagation. Notwithstanding that a transgenic plant may have been evaluated under confined field trial and accepted for environmental release in a foreign country, in order to satisfy Japanese guidelines it must also be subject to confined field trial evaluation in Japan.

Environmental safety evaluations for commercial release consider the molecular characterization of the transgenic plant, its reproductive and propagative properties including potential outcrossing, tendency to weediness, production of toxic substances, and other physiological characteristics. In the case of non-food organisms, immediate commercialization is possible, otherwise compliance with Ministry of Health and Welfare guidelines is also required.

5.3.4 Food Safety

To date, the safety assessment of GE foods has been conducted based on the voluntary "*Standards for Safety Assessment of Foods and Food Additives Produced by Recombinant DNA Techniques*", which are administered by the Ministry of Health and Welfare. These guidelines apply specifically to:

- a seed plant produced by recombinant DNA techniques used as food; or
- foods or food additives obtained through the use of non-pathogenic microorganisms produced by recombinant DNA techniques.

Food products derived from plants produced through clonal propagation or any forms of selection are specifically excluded from consideration under the guidelines.

The food safety risk assessment is built upon the principle of substantial equivalence and seeks to compare the new food product with a traditional counterpart, focusing on the defined differences between the two. The criteria examined are consistent with those applied internationally, and include:

- information on genetic materials including classification and origin of the host plant (including known allergenicity, toxicity or anti-nutritive properties), donor organism (including known allergenicity or pathogenicity), and properties of the inserted gene(s);

- human dietary exposure to the host plant including history of consumption;

- compositional analysis of the new food product compared with the traditional food, including the presence of toxins and antinutrients; and

- information on any differences in usage, processing, or anticipated consumption patterns between the new product and its traditional counterpart.

In situations where the safety of the GE food cannot be established based on substantial equivalence, additional data may be required. These include studies on: acute toxicity; chronic toxicity; mutagenicity; carcinogenicity; and intestinal, immunological or neurological toxicity.

The examination of safety assessments is done in consultation with the Food Safety Investigation Council and the resulting decisions are published. There are no provisions for pre-approval public notification of assessments under examination or the solicitation or consideration of public input.

As of December 1999, 29 foods and 6 food additives have been evaluated based on the standard for safety assessment and recognized as safe by the Ministry of Health and Welfare.

5.3.5 Post-Market Considerations

Under a revised Japanese Agricultural Standard (JAS) law, all GE food products must be labelled as such beginning in April 2001. These labelling requirements will apply to all products containing detectable recombinant DNA or transgenically expressed protein above a threshold of 5%.

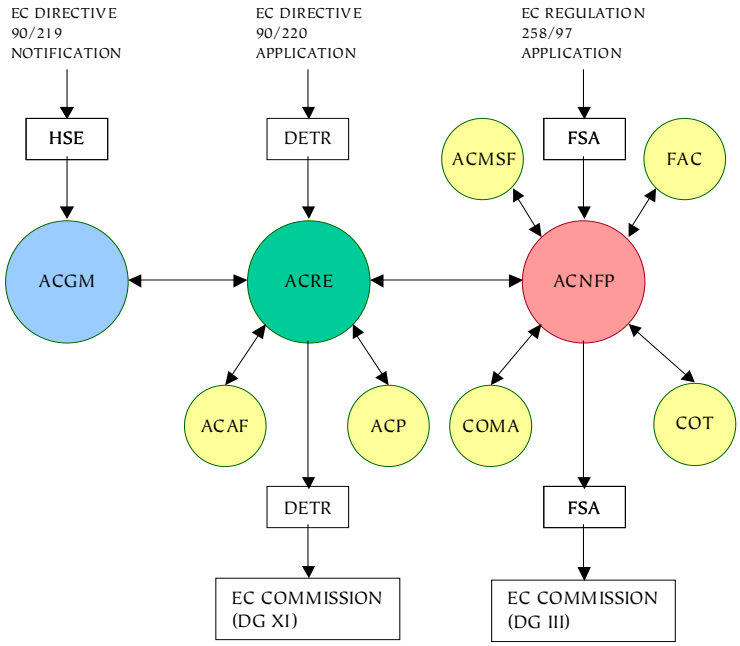
5.4 United Kingdom

5.4.1 Overview

In 1978, the United Kingdom (UK) was the first country in the world to pass legislation controlling genetic modification in a laboratory setting (NCBE 2000). These regulations required anyone performing genetic manipulation work to notify the Genetic Manipulation Advisory Group, which was replaced in 1984 by the Advisory Committee on Genetic Modification (ACGM). This non-statutory body still advises the Health & Safety Executive (HSE) on the contained use of GMOs (Fig. 3).

The first piece of primary legislation in the UK dealing specifically with the environmental release of GMOs (SCEC 1998) was Part VI of the Environmental Protection Act 1990, which was passing through Parliament concurrently with the European Commission development of proposals to control GMOs. This latter activity resulted, in April 1990, in two Directives on contained use (90/219/EEC) and deliberate release (90/220/EEC). Since February 1993, the deliberate release of GMOs has been regulated under the Environmental Protection Act 1990 and the GMO (Deliberate

Fig. 3 Relationship between the main advisory committees and UK regulatory authorities responsible for agricultural biotechnology.



ACAF - Advisory Committee on Animal Feedingstuffs
ACGM - Advisory Committee of Genetic Modification: Advises on all aspects of human and environmental safety of contained use (e.g., laboratory) of GMOs.
ACMSF - Advisory Committee on Microbiological Safety of Food
ACNFP - Advisory Committee on Novel Foods and Processes: Considers the safety of foods derived from GMOs.
ACP - Advisory Committee on Pesticides
ACRE - Advisory Committee on Releases to the Environment: Considers the environmental safety of field trials and the marketing of GMOs.
COT - Committee on Toxicity
COMA - Committee on Medical Aspects of Food Policy
DETR - Department of Environment, Transport and Regions
FAC - Food Advisory Committee
FSA - Food Standards Agency
HSE - Health and Safety Executive

Release) Regulations (1992). These latter regulations are the vehicle for implementing Directive 90/220/EEC.

Directive 90/220/EEC (EPCEU 1990) and the UK Regulations both apply to the environmental release of all GMOs, whether microorganisms, plants, or animals, but not to organisms obtained by "conventional" breeding techniques, including accelerated mutagenesis. The scope of Directive 90/220/EEC does not extend to products derived from GMOs, such as paste or ketchup from a genetically engineered tomato. In addition, the approval for placing on the market of a GMO is in respect of a specific use, such as import and processing, and does not automatically imply approval for commercial scale cultivation.

The deliberate release Directive (90/220/EEC) imposes a notification requirement and specifies the information that must be provided to the competent national authorities. In the UK, the responsible authority is the Department of the Environment, Transport and the Regions (DETR), which provides the secretariat for the Advisory Committee on Releases to the Environment (ACRE). ACRE is an independent statutory advisory committee, appointed by the Secretary of State for the Environment, which reviews applications for field trials or general (commercial) releases of GMOs under parts B and C of Directive 90/220/EEC. Applications for consent are required to contain information covering all aspects of the proposed release, and in particular, provide a detailed environmental risk assessment. It is also important to note that ACRE does not itself prepare the environmental risk assessment for the proposed release, but rather provides its advice based on a review of the proponent's environmental assessment.

The legislation requires that detailed information about each release application and consent is made available to the public, and Ministers are required to keep a statutory public register of such information. ACRE also publishes information on its deliberations and advice to Ministers on its website. However, there are no formal requirements to solicit and/or consider public comments during the review of an application for environmental release.

The European Commission published a draft revision to Directive 90/220/EEC in February 1998. While a complete discussion of the proposed amendments is beyond the scope of this document, some of the main elements include: clarification of principles upon which risk assessments should be based, including entrenchment of the precautionary principle; post-market monitoring to include "any relevant direct, indirect, immediate or delayed effects on human health and/or the environment"; and the introduction of a seven year time period for marketing approvals with provisions for reapplication and renewing consents. There is an expectation that the revised Directive will be agreed by the European Parliament by the end of 2000.

For the moment there is no specific Community legislation on GE derived livestock feed and the eight GE products authorized for such use have been approved in accordance with Directive 90/220/EEC. The introduction of draft legislation dealing specifically with GE feeds is anticipated in the fall of 2000.

On May 15, 1997, the European Community's Novel Foods Regulation (EC 258/97) came into effect and introduced a mandatory pre-market approval system for novel foods, and novel food ingredients, throughout the European Union (EPCEU 1997). These regulations, which are legally binding on all Member States, superseded the marketing consent for food GMOs previously covered by Directive 90/220/EEC, and introduced requirements for safety assessment, environmental risk assessment (for GMOs) and labelling of products. Under the Novel Foods Regulation, developers wishing to market a novel food are required to submit an application to the competent authority in the Member State where they first intend to market their product. Since April 1, 2000, the competent UK authority has been the newly created Food Standards Agency (FSA), which takes over this function from the Ministry of Agriculture, Fisheries and Food, and the Department of Health.

The new Food Standards Agency is accountable to Parliament through Health Ministers and through the equivalent devolved authorities in respect of the Scottish Parliament and National Assembly for Wales. The Agency operates at arms-length from Ministers under the day-to-day responsibility of a Chairman (currently, Sir John Krebs), a Deputy Chairman and 12 Board members. As indicated from its name, the Agency is not involved in the inspection or enforcement activities related to food safety. In taking over the government's food research and surveillance programmes, the FSA will be working to develop and improve the current risk procedures and science base that underpin existing regulations and standards.

The Advisory Committee on Novel Foods and Processes (ACNFP), originally established in 1988 as an independent panel of scientific experts, is a non-statutory body that provides advice to the competent UK authorities on all matters relating to novel foods, and novel food processes including food irradiation (FSA 2000). For the purposes of regulation, a novel food includes any food that has no significant history of human consumption within the Community prior to May 1997, and has been derived from, or contains, the products of genetic engineering, or is the result of a new method of production that significantly changes its composition or nutritional attributes.

When assessing a novel food, the ACNFP bases its safety assessment on the concept of substantial equivalence. Similarities and more importantly, differences between the novel food and the existing food are identified and examined carefully. The Committee then decides whether the novel food can be considered equivalent to, and

therefore as safe as, the existing food. During the course of its deliberations, ACNFP consults with a number of other advisory bodies, including ACRE. ACNFP's advice to FSA must also be forwarded to the European Commission and other Member States, who must agree with the determination, before final approval can be given.

In a new measure designed to increase public disclosure and regulatory transparency, amendments to the UK regulations were announced in December 1999 that enable ACNFP to make public all information submitted to it as part of an application under EC 258/97. Exceptions include information which:

- is not required by the guidelines accompanying the EC Novel Foods Regulation;
- has been agreed by the ACNFP Secretariat to be confidential because disclosure would harm competitive position; or,
- has been agreed by the ACNFP Secretariat to be confidential because disclosure would harm intellectual property rights (IPR).

This initiative will offer the public the opportunity to submit comments that ACNFP may consider as part of their deliberations. The ACNFP's draft conclusions will also be offered for comment before being finalized. As with other advisory committees, such as ACRE, ACNFP publishes an annual report (ACNFP 1999) that details the applications considered, advice to Ministers, and other related activities.

In May 1999, the UK Government announced the outcomes of a review of its regulatory framework for biotechnology (OST 1999), one of which was the establishment of the new Agricultural and Environment Biotechnology Commission (AEBC). The AEBC will have a wide-ranging remit to take a strategic view of developments in biotechnology and address broader issues including ethical considerations regarding the acceptability of genetic engineering.

5.4.2 Innovation and Scientific Discovery

The European Commission's (EC) contained use Directive (90/219/EEC), which covers only genetically modified microorganisms, has been implemented more broadly in the United Kingdom (UK) as the GMO (Contained Use) Regulations 1992. The aim of these regulations is the protection of "persons against risks to their health, whether immediate or delayed, and the protection of the environment". Although their scope is wider than the EC Directive, extending to activities involving any GMOs (as well as animal and plant cell cultures), the provisions relating to the protection of the

environment apply only to genetically modified microorganisms. For higher order GMOs, such as plants and animals, the regulations only cover risks to human health.

The main requirements of the control regime established by the Contained Use Regulations are: to carry out a prior assessment of the risks to human health and environment arising from any activity involving genetic manipulation and to maintain appropriate records; to notify the Health and Safety Executive (HSE) of an intention to use premises for the first time for genetic manipulation work (and for some activities to await for HSE consent); and to notify the HSE of individual activities involving genetic manipulation. There are allowances to consider a single notification for multiple activities at a single site, or a single activity carried out at multiple sites by one individual. Once HSE has been notified of an intention to use a premises for the first time, there are no further requirements for notification for subsequent activities involving Group 1 organisms (*e.g.*, most animals and plants), which are unlikely to cause disease to humans, animals or plants, or cause adverse effects in the environment.

5.4.3 Environmental Release

Directive 90/220/EEC defines two types of release applications depending on their intended purpose:

- **Part B applications:** Mainly for research and development trials. They are submitted to ACRE and consent is given at the national level; and

- **Part C applications:** For placing a GMO on the EU market (Fig. 4). These applications are made initially to the EU Member State in which the first release is planned. After reviewing the dossier and if satisfied, the lead Member State forwards the application to the European Commission with a favourable opinion. The other 14 states then also review the dossier, and if objections are raised that cannot be resolved the application is subjected to a more elaborate decision making process by the European Commission, otherwise the originating country issues the consent.

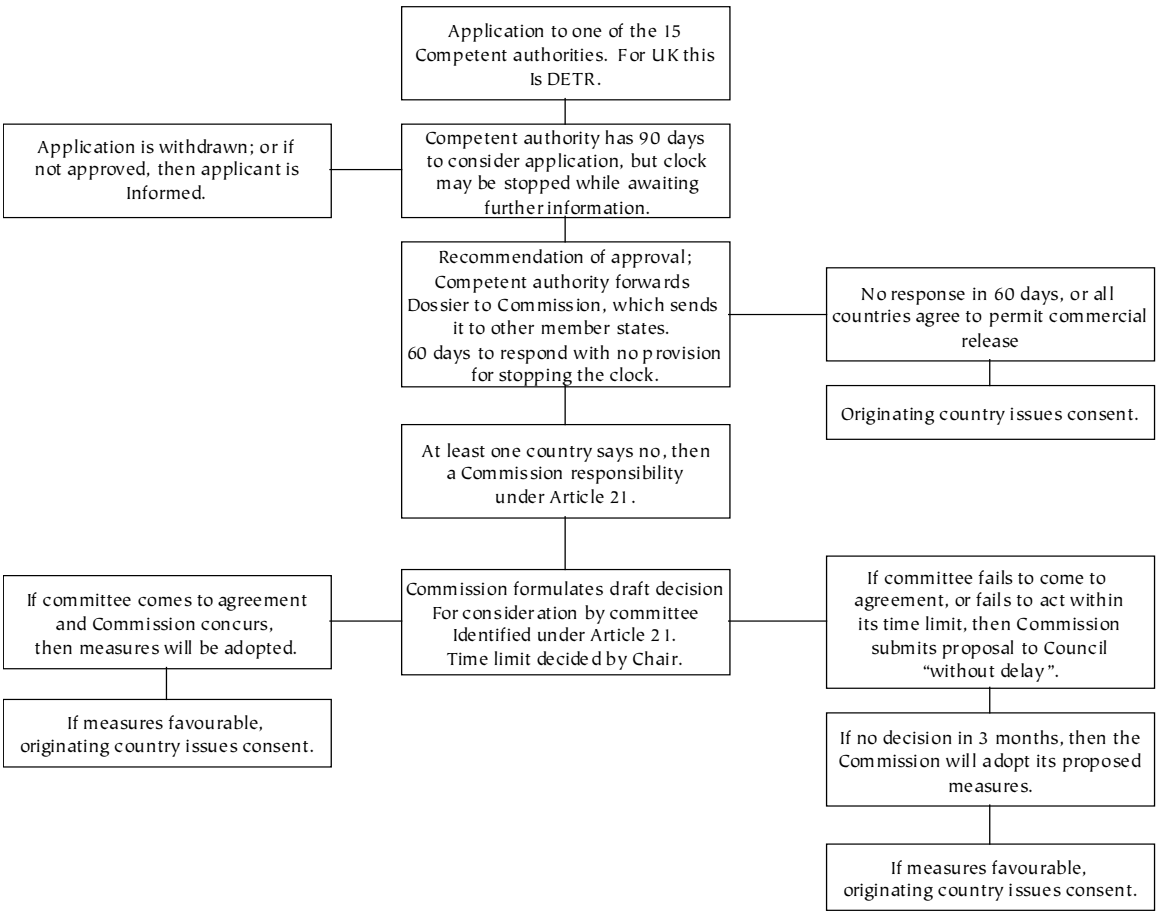
  The Commission seeks the opinion of its Scientific Committees (Scientific Committee on Plants; SCP) before drafting a proposed decision, which is put forward to a committee composed of representatives of Member States. This committee is chaired by a representative of the Commission, who decides on the time limit for deliberation based on the urgency of the matter (so called Article 21 committee). If there is agreement, by a qualified majority vote, and the measures recommended by the committee are acceptable by the Commission, then they are adopted. If these measures are favourable, the originating country issues the consent. However, if the committee identified in

Article 21 fails to come to agreement, or takes no action, then the Commission shall submit a proposal to the Council "without delay". Again, if there is no decision within 3 months the Commission adopts its proposal, which if favourable allows the originating country to issue the consent. Once issued, Part C consents apply across the whole European Community.

Anyone wishing to release a GMO into the environment must submit an application to ACRE that includes a detailed environmental risk assessment. ACRE has published guidance to developers that indicates the risk factors that should be considered during the preparation of their environmental assessment. These typically include characterizations of: the recipient or parental organism(s); the genetic modification(s), be it the inclusion or deletion of genetic material, and relevant information on the vector and the donor; the GMO; the intended release or use including its scale; the potential receiving environment; and the interaction between these.

For farm-scale field trials, ACRE's review process generally takes up to 90 days, but DETR has implemented "fast-track" procedures in certain cases. These include proposals that are low hazard, low risk, or repeat trials for particular organisms that

Fig. 4 Schematic of the regulatory approval process under Part C of Directive EC 90/220



have previously been approved. In these cases, the application is processed in 30 days and does not include a review by ACRE. ACRE publishes a status report of applications reviewed under Parts B and C of Directive 90/220/EEC in its Annual Report (ACRE 1999) as well as summaries of other issues considered during the past year. This information, including all deliberations and advice to Ministers, is available on ACRE's website. There are no statutory requirements for soliciting public input or considering broader social issues during the course of a review.

Since the Deliberate Release Regulations came into force in 1993 and up until December 1999, ACRE has provided advice on 175 field trials of GMOs. Under the Environmental Protection Act 1990, field trials are subject to inspection by the Health and Safety Executive, which is responsible for ensuring that the terms and conditions of authorization as prescribed by ACRE are adhered to by developers. To date, there are no commercial plantings of genetically engineered plants in the UK.

The UK philosophy is that tests of new crops should be conducted "a step at a time" and that the scale of use should be increased gradually only as it becomes apparent that it is safe to do this. The implementation of a revised Directive 90/220/EEC will impose even stricter requirements for developers to assess the potential "direct, indirect, immediate and delayed" consequences of released GMOs. In meeting the requirements for evaluating "delayed effects" (*i.e.*, effects on human health or the environment which may not be observed during the period of the release but become apparent as a direct or indirect effect either at a later stage or after termination of the release), developers will have to implement extensive monitoring and surveillance programs. Experience and data gained through the monitoring of experimental releases of GMOs may assist in designing the post-market monitoring scheme for the placing on the market of GMOs as, or in, products.

5.4.4 Food Safety

For a full safety assessment, developers are required to submit an application to the competent authority in the Member State where they first intend to market the product (*i.e.*, FSA in the UK). A copy of the application must also be sent to the European Commission. Once the competent authority has accepted the application, it has 90 days in which to complete an initial safety assessment and forward it to the Commission. The assessment is then copied to each of the other Member States, who have 60 days in which to comment. If the initial assessment is favourable and no objections are raised by other Member States, then the food product can be marketed throughout the European Union. If objections are raised the application will be referred to the EC Standing Committee for Foodstuffs for final agreement, consulting with the EC Scientific Committee for Food as necessary.

As a derogation from the full safety assessment procedure, Regulation (EC) 258/97 provides for a simplified procedure for GE foods that no longer contain GMOs and which are "substantially equivalent" to an existing food or food ingredient as regards to composition, nutritional value, metabolism, intended use and toxicology. In such cases, the developers only have to notify the European Commission when placing a product on the market together with either scientific justification that the product meets the criteria or an opinion to that effect from the competent authorities of a Member State. It is the opinion of ACNFP that only those products that contain no DNA or protein and which are not themselves genetically engineered qualify. Up until April 2000, 11 products had been notified to the Commission as being substantially equivalent, and no products consisting of, or containing, live GMOs had been approved under the full authorization procedure provided under Regulation (EC) 258/97. However, under Directive 90/220/EEC, two GE food plants had been approved for placing on the European market prior to the Novel Foods Regulation coming into force.

In assessing the safety of a GE food or food ingredient, ACNFP bases its evaluation on the same comparative approach adopted by several other regulatory agencies and considers a number of issues, including:

- toxicity of the inserted genes and the products of the inserted genes;
- allergenicity of the products of the inserted genes, including a consideration of the allergenicity of the host organism as well as that of any organisms used as sources of the inserted genes;
- transfer of genes encoding antibiotic resistance;
- nutrition, including composition and changes in levels of nutrients and the potential effects on the overall diet of replacing a conventional food with the GE one.

5.4.5 Post-Market Considerations

The first European Community regulation (1139/98) to control the labelling of food and food ingredients containing GE soy and maize (novel DNA or protein) was implemented in the UK in March 1999. This regulation has been amended to increase its scope to include foods sold to mass caterers and to introduce a 1% threshold trigger for labelling. The amended regulation came into effect in April 2000 as Regulation EC 49/2000. The aim of the threshold is to ensure that food ingredients obtained from non-GE sources do not need to be labelled as GE if they contain low levels (< 1% for each ingredient) of GE material because of accidental contamination.

These same provisions apply to additives and flavourings that may have been sourced from GE material (EC 50/2000).

5.5 United States

5.5.1 Overview

Regulatory oversight of biotechnology has been in place in the United States (US) for longer than in most other parts of the world. The first environmental release of a GMO occurred in 1983 following the approval of the National Institutes of Health (NIH). This first release was a field test of "ice-minus" bacteria used for preventing frost damage on strawberries. These were strains of *Pseudomonas syringae* and *Erwinia herbicola* with mutations in a gene encoding an ice-nucleation protein that is normally expressed on the bacterial cell surface, but not in "ice-minus" strains. This approval sparked a heated controversy, including several court cases, challenging the NIH decision and questioning the ability of federal agencies to address hazards to ecosystems in light of the uncertainties.

Table 5: US regulatory authorities for crop biotechnology products.

Agency	Jurisdiction	Laws
USDA	Plant pests, plants, veterinary biologics	Federal Plant Pest Act (FPPA)
FDA	Food, feed, food additivies, veterinary drugs, human drugs, medical devices	Federal Food, Drug, and Cosmetic Act (FFDCA)
EPA	Microbial and plant-pesticides, new uses of existing pesticides, novel microorganisms	Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA); FFDCA; Toxic Substances Control Act (TSCA)

In 1984, a White House committee was formed under the auspices of the Office of Science and Technology Policy (OSTP) to propose a plan for regulating biotechnology. This plan, published by the OSTP in 1986 as the *Coordinated Framework for the Regulation of Biotechnology*, is still in use today. It is based on the principle that techniques of biotechnology are not inherently risky and that biotechnology should not be regulated as a process, but rather that the products of biotechnology should be regulated in the same way as products of other technologies (OSTP 1992). The framework outlined roles and policies of the federal agencies and contained the ideas that:

- existing laws were, for the most part, adequate for oversight of biotechnology products;
- the products, not the process, would be regulated;
- genetically engineered organisms are not fundamentally different from non-modified ones; and

- oversight authority should be exercised only where there is evidence that the risk posed by the introduction is unreasonable.

Three US agencies share responsibility for regulating agricultural biotechnology (Table 5). The Animal and Plant Health Inspection Service (APHIS) of the US Department of Agriculture (USDA) is responsible for ensuring that the growth of genetically engineered plants does not harm the agricultural environment (as distinct from the wild environment). The Environmental Protection Agency (EPA) is responsible for assuring the human and environmental safety of pesticidal substances engineered into plants, and the Food and Drug Administration (FDA) is responsible for assuring that foods derived through genetic engineering are as safe as their traditional counterparts.

Products are generally regulated according to their intended use, with some products being regulated under more than one agency (*e.g.*, pesticidal plants). Notwithstanding this overall product focus, the trigger for regulatory oversight, at least with respect to the environmental release of plants derived via biotechnology (USDA-APHIS) and the registration of plant-pesticides (EPA), is the process of genetic engineering. The same degree of scrutiny is not applied to these products derived through traditional breeding, selection, or accelerated mutagenesis.

Before commercialization, genetically engineered plants/organisms must conform with standards set by State and Federal marketing statutes such as State seed certification laws, the Federal Food, Drug and Cosmetic Act (FFDCA), the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the Toxic Substances Control Act (TSCA), and the Federal Plant Pest Act (FPPA). There are no national requirements for varietal registration of new crops.

The USDA is the lead agency for regulation of genetically engineered plants, including the environmental release of these products in confined field trials. In 1993, USDA finalized a regulation that described a petition process for determining that particular plants would no longer be regulated and, therefore, could be commercially planted (USDA 1993a). Regulated articles are defined by USDA-APHIS as plants or microorganisms that are, or are believed to be, plant pests or are produced using plant pests. APHIS authority to regulate genetically engineered plants stems from the fact that, to date, they have been products of *Agrobacterium tumefaciens* (a bacterial pest causing crown gall disease in plants) mediated transformation and/or contain regulatory sequences derived from a plant pest (*e.g.*, cauliflower mosaic virus 35S promoter). The regulations are contained within 7 CFR (Code of Federal Regulations) Part 340, "*Introduction of Organisms and Products Altered or Produced Through Genetic Engineering Which are Plant Pests or Which There is Reason to Believe are Plant Pests*". For a crop to achieve nonregulated status, "environmental assessment"

and "determination of nonregulated status" documents are prepared by USDA that address a number of safety concerns including impacts on agriculturally beneficial organisms and the potential to become a plant pest.

In 1994, EPA proposed a rule to regulate the pesticidal substances in pest-protected plants as plant-pesticides under FIFRA and FFDCA. Under this proposal, which has yet to be finalized, EPA claims broad jurisdiction over such products in all transgenic seeds and plants sold with claims of pest-protection, but it grants a generic exemption from registration to those bred by conventional means. A plant-pesticide is defined by EPA as a "*pesticidal substance that is produced in a living plant and the genetic material necessary for the production of the substance, where the substance is intended for use in the living plant*".

Since it registered its first plant-pesticide in 1995, the EPA has been using approval and registration guidelines that were established for testing chemical, microbial, and biochemical pesticides. To date, EPA has granted tolerance exemptions to 12 plant pesticides, six of these are for *Bt* toxins produced in corn, potato, and cotton, and the remainder are for transgenically expressed plant virus proteins.

The purpose of EPA's proposed new rule is to focus regulatory oversight on plant-pesticides that create novel exposures or operate with a more toxic mode of action. It would: clarify the regulatory status of plants and plant-pesticides under FIFRA and FFDCA; specify that EPA regulates the plant-pesticide rather than the plant itself; and describe the categories of products subject to, and exempt from, regulation. Exemptions would be made for plant-pesticides derived from plants related to the recipient plant, those that act by affecting the plant, and those based on the coat protein of a plant virus. The focus of EPA's proposed rules clearly would be on the new pest-resistant varieties produced using genetic engineering.

Under the FFDCA, the FDA has the authority to require pre-market review and approval in cases where protection of public health is required, such as when a substance is added intentionally to a food and there are questions about its safety. FDA also has post-market authority to remove a food product from commerce and sanction those marketing the food if it poses a risk to public health. In the US, the complex array of criminal and civil sanctions, including tort and contractual remedies, available to governments and private parties provides food producers and manufacturers with every incentive to bring safe, wholesome foods to market.

In 1992, the FDA conducted its first, and only, comprehensive scientific review of a genetically engineered food product (FDA 1995). This was at the request of Calgene Inc., who had developed the Flavr Savr™ tomato by inserting an additional copy of the polygalacturonase (PG) encoding gene in the antisense (*i.e.*, backwards) orientation,

resulting in reduced translation of the endogenous PG messenger RNA (mRNA). The PG enzyme is the chief mechanism for pectin degradation in tomato fruit leading to fruit softening. The transgenic variety ripens normally but experiences less pectin breakdown and, therefore, has increased thickness and consistency that benefits all stages of harvesting and processing. In developing the Flavr Savr™ tomato, Calgene used the kanamycin resistance marker gene that encodes neomycin phosphotransferase II (NPTII), as a selectable marker. This was the only new protein expressed in the transgenic tomato.

In its evaluation of the Flavr Savr™ tomato, FDA considered the source, identity, function, and stability of introduced genetic material, compositional and nutritional studies, the safety of the NPTII protein, and the environmental safety of the use of the NPTII encoding gene. FDA's assessment concluded that the Flavr Savr™ tomato was substantially equivalent to, and as safe to eat as other tomatoes currently on the market. This assessment was supported by the agency's Food Advisory Committee, a panel of experts from outside FDA.

During this period, FDA published in the *Federal Registry* a Statement of Policy (1992) on its approach to the regulation of foods derived from genetically engineered plants. The purpose of this policy was to provide a risk-based "decision tree" to guide plant breeders and food manufacturers through issues critical to ensuring the safety, nutritional value, and wholesomeness of new foods. Under this "standard of care", which applies equally to new foods produced through traditional breeding as well as biotechnology, FDA also provided guidance on regulatory issues such as when an introduced substance is not generally recognized as safe and would require pre-market approval as a food additive, and when special labelling would be required under FFDCA. Food producers are not required to seek FDA pre-market approval or apply a special label for a new variety of food if it is substantially equivalent to existing varieties already on the market.

The cornerstone of FDA's 1992 policy is that foods produced as a result of genetic engineering are not inherently more risky than foods produced through more conventional means. Since publishing this policy, FDA has conducted its reviews of genetically engineered foods by consulting with companies about the safety and composition of the variety, and has not required a food additive petition for any other transgenic product, although it could make such a request in the future. Under the guidelines for this voluntary consultation process, which were published by FDA in 1997, developers of food products from transgenic plants are asked to provide summary information of their safety and nutritional assessment, and to make a scientific presentation of their data to FDA scientists. Without exception, all developers of genetically engineered foods have participated in this voluntary scheme and, to date, FDA has completed 45 consultations.

In May 2000, the Clinton Administration announced a number of new initiatives geared toward reinforcing the strength and transparency of the regulatory system, and enhancing the information provided to consumers and farmers (FDA 2000). Among these were:

- a review of Federal environmental regulations by the Council on Environmental Quality and the OSTP;

- steps to be taken by the FDA to implement a requirement for mandatory notification at least 120 days before any new agricultural biotechnology crops or products are introduced into the food supply, and to propose that submitted information and the agency's conclusions be made available to the public;

- the addition by FDA of more scientists with agricultural biotechnology expertise to its food and veterinary medicine advisory committees;

- guidelines to be developed by the FDA for voluntary efforts to label food products under their authority as containing or not containing bioengineered ingredients in a truthful and straightforward manner; and

- actions by the USDA to provide farmers with reliable information on markets and best farming practices for new crop varieties.

5.5.2 Innovation and Scientific Discovery

The Department of Health and Human Service's National Institutes of Health (NIH) established the Recombinant DNA Advisory Committee (RAC) in October 1974 in response to public concerns regarding the safety of DNA manipulation techniques. A that time, it was thought that, "The use of this technology has various possible hazards because new types of organisms, some potentially pathogenic, can be introduced into the environment if there are no effective controls."

The RAC developed a set of Guidelines that were first published in 1976 and have been revised periodically since then. The purpose of the NIH Guidelines is to describe facilities and practices intended to prevent unintended release or inadvertent exposure to either genetically modified organisms (GMOs) or recombinant DNA. While these guidelines are voluntary and are widely followed by academic and industrial scientists around the world, they are mandatory for any research that receives support from NIH, including research performed directly by NIH.

5.5.3 Environmental Release

In considering an application to conduct a field trial, APHIS examines a number of criteria including: stability of the inserted genetic material (*e.g.*, genomic integration vs plasmids, viral vectors, or transposable elements); the possibility of the introduced genetic material mediating plant, animal or human disease, or the production of infectious entities; the possible impact of the plant on the environment including endangered or nontarget species; the precautions taken to prevent the escape of pollen, plants, or plant parts from the field trial site; and the purpose of the test. If the agency reaches a Finding of No Significant Impact (FONSI) during its preparation of an Environmental Assessment, a permit is issued (Table 6).

Table 6: Product movement through the US regulatory system.

Research & Development	- Compliance with NIH Guidelines for work with GMOs is mandatory for all scientists receiving federal funding or working for federal agencies.
Field Trials	- Following a letter of notification, developers must receive APHIS approval for field trials and submit summary reports. - Trials may be inspected by APHIS and/or state department of agriculture officials. - Developers must comply with APHIS performance standards developed to minimize "outcrossing" and inadvertent environmental release. - APHIS also oversees transport of seed to and from trial site. - For trials of pesticidal plants >10 acres, need an Experimental Use Permit from EPA. Public notification and comment is required here, but not for field trials generally.
General Environmental Release	- Developers must apply to APHIS for a determination of non-regulated status. Public notification and comments solicited. - APHIS review (>=10 months) considers range of risk factors including environmental effects, wildlife effects, and potential to become a plant pest. - For pesticidal plants (e.g., Bt corn), the plant-pesticide substance [e.g., Cry1A(b)] must be subject to risk assessment (>= 18 months) and registration by EPA. Public notification and comment is invited through publication in the *Federal Register.*
Use as Food	- Through its voluntary consultation process, FDA works with the producer from an early stage in product development to ensure that all food safety issues have been addressed. - Based on a favourable review of summary data and a presentation to FDA scientists, FDA issues a letter stating they have no further questions.
Post Commercialization	- All three regulatory agencies have the legal power to demand immediate removal from the marketplace of any product should new, valid data indicate a question of safety for consumers or the environment.

In 1993, in an effort to streamline its procedures, APHIS introduced a notification alternative to the environmental assessment and permit procedure for environmental releases in field trials (USDA 1993b). The notification process, which originally applied only to transgenic tomato, corn, tobacco, soybean, cotton or potato, was amended in 1997 to include any plant species not listed as a regulated noxious weed and not considered a weed in the area of the proposed release. Instead of submitting a formal application for a permit, plant breeders submit a letter of notification to APHIS, which includes a description of the gene, the characteristics of the plant, and the location of the proposed tests. As part of this procedure, APHIS then notifies the department of agriculture in the state where the proposed trials will be conducted.

APHIS does not engage in a public consultation process related to environmental releases in field tests, but does periodically publish a notice in the *Federal Register*

indicating the availability of a listing of current field trials. As a rule, APHIS does not impose limitations on the size of field trials. Specific performance standards have been developed to maintain reproductive isolation and minimize inadvertent escapes during the conducting of a field test.

For field tests of transgenic plants expressing plant-pesticides (*e.g.*, *Bt* toxins, viral coat proteins) greater than 10 acres in size, the developer requires an Experimental Use Permit (EUP) from EPA, and is expected to consult with EPA staff to decide upon the supporting data requirements. In the process of considering an application for an EUP, the public is notified and comment is invited through publication in the *Federal Register*.

Before a genetically engineered crop can be produced on a wider scale and sold commercially, its creators must petition APHIS for a "determination of non-regulated status". APHIS has published a "*Guide for Preparing and Submitting a Petition for Genetically Engineered Plants*" that uses a case-study approach to describe the nature and format of field test data that must be provided (USDA 1996).

The type of information considered includes: the biology and genetics of the host plant including methods of reproduction, tendency to weediness, and modes of gene escape; a complete molecular characterization of the transgenic plant (in line with the Canada - US harmonized molecular characterization requirements); and the environmental consequences of introducing the transgenic plant including any changes in potential for weediness, impacts on nontarget organisms, or horizontal gene transfer that would be a consequence of the genetic modification.

Upon receipt of a petition, APHIS publishes a notice in the *Federal Register* soliciting public comment as to whether the regulated article presents a plant pest risk. This notification includes a synopsis of the petition (*i.e.*, general characteristics of the transgenic plant) and explains the role of other regulatory bodies (EPA and FDA), and the process for submitting comments and obtaining more information, including a copy of the petition, less any confidential business information.

Following its assessment, and if it determines that the plant poses no significant risk to other plants in the environment and is as safe to use as more traditional varieties, APHIS publishes a "determination of non-regulated status" in the *Federal Register*. This notice advises the public of the availability of all written comments received, APHIS's environmental assessment, and FONSI for the article.

For plants with pesticidal properties, such as *Bt* corn, APHIS coordinates its review with the EPA, who is responsible for the regulation of pesticidal substances under FIFRA and FFDCA. In addition to examining data on product characterization (*e.g.*, source of

the gene; its expression; nature of the pesticidal substance produced; modifications to the introduced trait as compared to that trait in nature; biology of the recipient plant; effects on nontarget organisms; exposure; and environmental fate), EPA also requires data on toxicology, digestive fate, and potential allergenicity of the pesticidal substance. Proposed registrations of plant-pesticides are subject to notification and a period of public comment.

5.5.4 Food Safety

Food producers in the US have the legal responsibility to ensure the safety of foods they offer consumers. The goal of FDA's voluntary consultation process is to work together with developers, beginning at an early stage in product development, to identify and resolve any issues regarding the food that would necessitate legal action by the agency if the product were introduced into commerce. Examples of such issues include significantly increased levels of plant toxicants or antinutrients, reduction of important nutrients, the presence of new allergens, or the presence in the food of an unapproved food additive. When the developer has accumulated the data that it believes are adequate to ensure that its product is safe and complies with the relevant provision of the Act, the developer submits a safety and nutritional assessment summary to FDA that typically includes:

- the purpose of intended technical effect of the modification on the plant, together with a description of the various applications or uses of the bioengineered food, including animal feed uses;

- a molecular characterization of the modification including the identities, sources and functions of introduced genetic material;

- information on the expressed protein products encoded by introduced genes;

- information on known or suspected allergenicity and toxicity of expressed products;

- information on the compositional and nutritional characteristics of the food, including antinutrients;

- for foods known to cause allergy, information on whether the endogenous allergens have been altered by the genetic modification; and

- in some cases, the results of comparisons of wholesomeness feeding studies with foods derived from genetically engineered plants and the non-modified counterpart.

In keeping with the voluntary nature of this process, there are no requirements for public notification in the *Federal Register* or public consultation. In such a case, FDA does not issue a product approval *per se*, but informs the developer by letter that it has no further questions based on the information presented, and reminds the developer of its legal responsibilities. FDA does publish a list of completed consultations that identifies the name of the developer, the introduced trait, the source and identity of any introduced genes, and the year in which the consultation was completed.

5.5.5 Post-Market Considerations

While there have been no substantiated cases of field developed insect resistance to *Bt* crops, it is generally recognized that some form of insect resistance management (IRM) is key to the sustainable use of *Bt* toxins in both transgenic crops and *Bt* microbial spray formulations. The EPA does not generally make pest resistance management mandatory for all pesticides. However, because of the special "public good" case posed by *Bt* microbial sprays, which have been registered for use since 1961 and used extensively in organic agriculture as part of integrated pest management programs, the EPA has indicated that these products are worthy of extra protection. Even though EPA has not formally published a policy or data requirements for IRM overall, general guidance has been provided to registrants on the essential elements necessary for an IRM plan, and the Agency has issued a joint EPA-USDA position paper on IRM in *Bt* crops.

On April 19, 1999, a biotechnology industry group submitted an IRM plan to EPA, and on January 14, 2000, EPA announced new measures for resistance management in *Bt* corn for the 2000 growing season that mirrored the industry plan. It directs registrants to ensure that growers maintain refugia of at least 20% non-*Bt* corn (50% in areas where cotton is grown). In addition, EPA imposed requirements for monitoring, remedial action, grower education, sales reporting, and development, collection and reporting of IRM research data.

Mandatory refuges for some other *Bt* crops, such as *Bt* cotton [Cry1A(c)] and *Bt* potato (20% structured refuge of non-*Bt* potatoes) have been in place since 1995 and 1999, respectively.

6 Summary Comparison of Regulatory Systems

As an aid to meaningful comparison of the different regulatory systems, six key comparators were identified. These were:

- legislative basis and public accountability;
- philosophical approach and regulatory triggers;
- transparency of the policy making and regulatory decision making processes;
- approaches to risk assessment;
- independence of the regulatory decision-making process; and
- the role of post-market surveillance.

This summary comparison presents a brief description of the significance of each comparator in the context of Canada's regulatory framework for biotechnology and highlights significant similarities and differences with the approaches taken in other countries.

6.1 Legislative Basis and Public Accountability

6.1.1 Existing legislation versus new technology-specific legislation

In Canada, biotechnology products are regulated nationally by the federal government under authority derived from at least 10 pieces of preexisting legislation (*Seeds Act, Feeds Act, Fertilizers Act, Health of Animals Act, Food and Drugs Act, Canadian Environmental Protection Act, Plant Protection Act, Consumer Packaging and Labelling Act, Patent Act*, and the *Pest Control Products Act*) that have been amended over time to deal with these new products. In regards to agricultural biotechnology, regulating the environmental release of plants with novel traits (PNTs) and their use in livestock feed is the responsibility of the Canadian Food Inspection Agency (CFIA). Health Canada is responsible for the human health safety assessment of novel foods. The Pest Management Regulatory Agency (PMRA), within Health Canada, provides expertise on pesticidal substances expressed in PNTs (*i.e.*, Bt toxins) that is used by CFIA during its risk assessment process. The Department of Fisheries and Oceans is currently developing regulations to govern the potential future environmental release of transgenic aquatic organisms.

Like Canada, the regulation of biotechnology products in the United States is based on preexisting legislation administered by the USDA (*Federal Plant Pest Act*), the EPA

(*Federal Insecticide, Fungicide, and Rodenticide Act; Toxic Substances Control Act*) and the FDA (*Federal Food, Drug, and Cosmetic Act*). The regulatory systems in Argentina, Australia, Japan and the United Kingdom are based either solely (Australia, UK), or partly (Argentina), on existing or proposed regulations specific to gene technology. Australia has proposed a new Gene Technology Bill to be passed in 2000 and Japan will be replacing its current voluntary system of guidelines with mandatory regulations taking effect in April 2001.

6.1.2 Pre-market notification

Like Canada, pre-market notification for environmental release and food usage is mandatory in Argentina, Australia, and the UK. This also applies to the environmental release of genetically engineered plants, including their registration as plant-pesticides if applicable, in the US. Even though Japan has had a system of voluntary guidelines up until now, and the US FDA engages in a voluntary consultation process with industry, there has effectively been pre-market notification for every product. Both of these latter situations will be changing in the near future. As stated previously, Japan intends to implement mandatory regulations in April 2001, and the US FDA announced in May 2000 its intent to require mandatory notification 120 days prior to marketing GE food products.

6.1.3 Multi-tiered government involvement

The product approval processes within Australia and the UK differ from the other countries examined in that they involve significant input from other levels of government. In the case of Australia, the implementation and enforcement of food safety standards are under the jurisdiction of the States and Territories, hence, the approval of novel foods requires the agreement of Health Ministers from the Commonwealth of Australia, the States and Territories, and New Zealand. Under the UK system, approval for the marketing of genetically engineered commodities, including their use in food and feed, requires multinational agreement within the European Community.

6.1.4 Public accountability

In order to ensure efficiency and effectiveness, regulatory systems must be subjected to some measure of ongoing evaluation against performance standards. These standards should reflect more than simply turnaround time, but should also define appropriate levels of scientific and technical capacity required by the competent authority. The Auditor General of Canada has the primary responsibility for reporting on federal government efficiency and effectiveness in all areas, including the regulation of biotechnology products. Of particular relevance to the regulation of biotechnology products, the *Commissioner of Environment and Sustainable Development*, who reports to the Auditor General, is responsible for monitoring the progress of government departments in integrating social, economic, and

environmental concerns to enhance sustainable development. Under the *Auditor General Act*, individuals may submit petitions about environmental matters in the context of sustainable development. Most recently, the Sierra Legal Defence Fund submitted such a petition to voice their concerns about the role of the federal government related to the release of GMOs into the environment. Other mechanisms for examining the performance of the regulatory system include reviews by advisory committees, such as the Canadian Biotechnology Advisory Committee, parliamentary committees, and expert panels, such as the Royal Society of Canada Expert Panel on Food Biotechnology.

Currently there are two reviews examining food regulatory processes in Australia. These are the Food Regulation Review (Blair review), which examined the impact of regulations on costs within the food sector and opportunities for improved clarity and efficiency, and the Regulatory Reform Taskforce. The Task force has been established to undertake a comprehensive review of the administrative arrangements for the regulation of public health and safety with regard to food, therapeutic products, chemicals, and gene technology. The Blair review reported in 1998 and senior government officials are now considering a response to this report. Because of this review, ANZFA's overall role and functions may change, thereby impacting on the nature and extent of ANZFA's health promotion role.

Similar mechanisms of review exist in the United States, where the General Accounting Office performs an analogous function to the Canada's Auditor General. The USDA, EPA and FDA have adopted a practice of soliciting advice from stakeholders, expert panels and the public on existing and proposed policies and rules.

In those countries that employ either statutory or non-statutory scientific advisory committees, such as Argentina (CONABIA), Australia (GMAC), and the United Kingdom (ACRE, ACNFP, others), additional visible performance measurement activities are related to committee member selection and reporting on committee activities. For example, members to the ACRE and ACNFP are selected by Ministers, upon recommendation by the respective Committee Secretariats, through an open interview and selection process. The external interests of Committee members are declared each year in the Annual Report, and membership is reviewed every 3 years with a usual maximum term of 6 years. These Committees also publish Annual Reports, which summarize the issues and applications considered during the previous year along with their recommendations to Ministers.

6.2 Philosophical Approach and Regulatory Triggers

6.2.1 The regulatory trigger

The trigger for Canadian regulatory oversight is the novelty of the product rather than the methods used in its production. Within its regulatory framework, Canada has adopted terminology and definitions that are unique among those countries currently regulating biotechnology products. Rather than referring to genetically engineered plants or genetically engineered food products, the guidelines and regulations refer to plants with novel traits (PNTs) and novel foods, respectively. The confined and unconfined environmental release of PNTs as well as their use in livestock feeds and/or human foods is each subject to specific regulation.

While it is generally acknowledged amongst scientists worldwide that product attributes define the associated risks, each of the other countries included in this comparison utilize the process of genetic engineering as the *de facto* trigger for regulatory oversight. The exception is the US FDA, which, since its first formal review of the Flavr Savr™ tomato in 1992 (at Calgene's request), has engaged in a process of voluntary consultation with developers which attempts to treat food products derived from biotechnology on a par with other new food products.

This difference in approach means that some products, such as the imidazolinone herbicide tolerant corn mentioned previously, are subject to regulatory oversight in Canada but not in other jurisdictions.

6.2.2 Research involving genetic manipulation

As a minimum, all countries have implemented guidelines specifying levels of physical containment and health and safety procedures to be followed when undertaking research involving genetic manipulation. The Medical Research Council of Canada (now Canadian Institutes of Health Research) "*Guidelines for the Handling of Recombinant DNA Molecules and Animal Viruses and Cells*" and "*Laboratory Biosafety Guidelines*" are examples of voluntary guidelines. These guidelines, like those developed by the United States National Institutes of Health Recombinant DNA Advisory Committee, are widely followed and compliance with them is generally a requirement for NIH funding and is mandatory for researchers working in federal laboratories. Both the United Kingdom and Argentina have entrenched similar guidelines in regulation. Australia's proposed Gene Technology Bill 2000 will give the current non-statutory *"Guidelines for Small Scale Genetic Manipulation Work"* published by the Genetic Manipulation Advisory Committee the force of law.

6.2.3 Controlling confined field trials

The initial environmental release of a genetically engineered plant, or plant with novel trait in Canada, as an experimental field trial is critical to generating the data needed

to evaluate agronomic performance and environmental impact. Between Canada and the US more than 11,000 confined field trials have been conducted since 1987 (5233 in Canada since 1988; 5778 in US since 1987). All of the countries examined have a system of mandatory notification and/or environmental risk assessment prior to the approval of experimental field trials, and have developed standards for reproductive isolation and monitoring in order to minimize any impact to the environment or accidental release of plant material. Since 1993, the United States has implemented a streamlined notification process for field trials that does not require an environmental assessment provided the host plant and the genetic modification meet certain criteria.

6.3 Transparency of the Policy Making and Regulatory Decision-Making Process

6.3.1 Policy and regulations

Canadian law requires that the process of rule making, whether as new or amended legislation, statutes, or regulations, be transparent and open to public input. Publication of the proposed change in the official Parliamentary journal, *Canada Gazette*, is the mechanism for alerting the public and soliciting comment. While not identical in every respect, similar consultative processes are followed in Australia, Japan, the UK and US when new or amended legislation or regulations are proposed.

Similar provisions do not generally exist with respect to the institutional decisions that generally govern the approval of new products of biotechnology in Canada. The opportunity for public input in advance of these decisions is nonexistent, or is solely in the form of public notification of the policy change. A notable exception to this general rule is the practice of the Pest Management Regulatory Agency of issuing Proposed Regulatory Decision Documents (PRDDs) prior to registrations of new active ingredients and registrations that may result in substantially increased use or exposure. These PRDDs provide a 45-day period of public comment.

The openness of the product approval processes in countries like the US is precisely because amendments to regulations are required (*e.g.*, petition to deregulate), thus triggering advertisement in the US *Federal Register* and a period of public comment. With the exception of its 1992 review of the Flavr Savr™ tomato, US FDA has not required a food additive petition for any transgenic food product, which is why FDA has not issued public notification or requests for comments in advance of the 44 other genetically engineered food products that have been placed on the US market since that review.

6.3.2 Guidance to industry

All of the countries, including Canada, publish risk assessment information requirements in order to guide developers in preparing their applications for

environmental, food and/or feed evaluation. In some cases, such as the USDA-APHIS "*User Guide for Petitions*", the guidelines include a summarized mock submission to exemplify the type of information required.

6.3.3 Advance notification and public comment

In Canada, summaries of regulatory decisions involving novel foods, the environmental release of PNTs, and the use in livestock feeds of products derived from PNTs, are made available to the public by the respective regulatory agencies via the Internet or upon request. For these products, there are no provisions for public notification of petitions currently under review, or for soliciting public comment in advance of a pending regulatory decision.

Only Australia and the United States have implemented product approval systems that require both public notification and a request for public comments prior to the final regulatory decision. Australia's system is more open than the US in a couple of areas. In Australia, the pre-notification process applies to confined field trial applications, applications for general environmental release, and food safety approval. By comparison, public pre-notification is not a requirement in the case of field trials in the United States, nor is it a component of FDA's voluntary consultation process with industry. While anyone can request copies and/or summaries of petitions for determination of non-regulated status (USDA) or registration of a plant-pesticide (EPA), Australia has taken the extra step of publishing draft risk analysis reports and seeking public comment prior to preparation of the final risk analysis report (ANZFA).

Within the UK, the issue of transparency is evolving. Both ACFNP and ACRE publish summaries of applications, including those currently under consideration. As well, interested persons may request copies of complete applications for environmental release (less any confidential business information) from the Department of Environment, Transport, and Regions, or in the case of food safety approval, the Food Standards Agency. Even though soliciting public comment is not a requirement within the process, members of the public can and do write to the secretariats with their comments, which are made available to the advisory committees. The Food Standards Agency has also recently announced its intention to make public all non-confidential information submitted to it as part of an application for food safety.

6.3.4 Confidential business information

Confidential business information (CBI) is an issue, and is seen by some as a major stumbling block to the public dissemination of environmental and food safety information for products undergoing review. In all cases, the petitioners (companies) are responsible for determining what is or not CBI. However, some governments have taken a more aggressive stance with industry in the interest of increased openness. In the UK for example, if ACRE or ACFNP consider that CBI in applications cannot be

justified then the application is sent back to the proposer with the requirement to remove from the CBI section any information that cannot be justified as being confidential. In some cases, details included in the CBI sections have been published (P. Dale, personal communication).

6.3.5 Confined field trials

In Australia and the UK, the same degree of public notification and comment is provided for any environmental release of a GMO, whether in a confined experimental field trial or as a general (commercial) release. Both Canada and the US treat these two situations differently, releasing less information in the case of field trials. For each field trial notification, USDA-APHIS publishes the name of the organism, the new trait(s) or introduced genes, the name of the proposer, the location of the trial by state, and the status of the application. By comparison, Canada only publishes summary statistics describing numbers of trials, crops species and traits on a yearly basis. Argentina and Japan both publish annual summary information for experimental trials that identifies the crop, the introduced trait, and the petitioner.

6.4 Approaches to Risk Assessment

6.4.1 Risk assessment process

Canadian regulators employ an evidence-based approach to risk assessment that considers only the additional scientifically defensible risks associated with a particular product, without consideration of possible benefits. The research, testing and/or surveillance required to fully characterize a product, including the magnitude of associated risks, is the responsibility of the proponent. Evaluations by regulatory officials are based on data supplied with the petition, or provided in response to additional requests, and within the context of an expert knowledge of the relevant scientific discipline. This latter consideration would include knowledge of pertinent peer reviewed reports and scientific literature from around the world.

Each of the countries in this comparison has, as a minimum, taken a "cautious approach" toward evaluating the safety of genetically engineered or novel foods. Safety assessments have been built on the principle that novel foods are comparable to existing foods and that the risk factors (*e.g.*, nutrients and their bioavailability, antinutrients, toxins, and potential for allergenicity) are the same for all foods, regardless of the technology used to produce them. Risk assessments have focused on the defined differences between novel and existing foods and the effects that expression of newly introduced genes have on existing risk factors. The European Union has announced its intention of going one step further, and adopting the so-called precautionary principle as an attempt to eliminate risk. Adoption of the precautionary principle is not consistent with existing practice in countries such as

Canada and the US, which do not treat the lack of evidence of harm as a justification for indecision.

6.4.2 Hazards

Regardless of the ideological or political differences in regulatory approach, the risk factors considered during an environmental or food safety evaluation are, respectively, the same for each of the countries examined in this comparison. For the most part, the scientific component of each country's risk assessment process is built on internationally accepted principles, such as familiarity and substantial equivalence. For example, in assessing the environmental risks posed by GMOs (PNTs in Canada) there are six main safety issues that have been proposed by the OECD, and which are considered by each regulatory system. These are gene transfer, weediness, trait effects, genetic and phenotypic variability, expression of genetic material from pathogens, and worker safety.

6.4.3 Safety data

Without exception, the developers of genetically engineered crops and novel foods have been responsible for conducting all of the research, testing, and monitoring necessary to establish the safety of their products. Direct additional or confirmatory testing of specific products by regulatory authorities has not been implemented in any of the countries examined in this comparison. Nonetheless, the applicant is not the sole source of relevant scientific information. As a rule, each of the regulatory agencies also consider information that may come from other sources, such as the general scientific literature, general technical information, independent scientists, other regulatory agencies, and international bodies. In many cases, regulatory authorities have and continue to invest in research targeted to address specific issues related to the environmental and food safety of GMOs.

6.4.4 Benefits and other factors

To date, assessing the potential risks associated with biotech crops and their products has proven much more straightforward than attempts to evaluate potential benefits. None of the regulatory systems examined here have implemented an overall systematic benefits consideration into their review processes, and there is no international consensus on the best approach. Benefits have generally been assumed to take care of themselves, as products without obvious benefits are unlikely to have value in the marketplace. The analysis of benefit is also a complicated affair because of the question of "benefit to whom?" -- the farmer, the consumer, the developer, the environment, etc. In the UK, the recently formed Agriculture and Environmental Biotechnology Commission (which has a similar mandate to Canada's CBAC) may consider the practicalities of including "benefits assessment" in future.

Other than in Argentina, where there is a requirement for a technical report by the National Office of Agrifood Markets on the potential economic impact of genetically engineered products, regulatory decisions in different countries do not overtly make allowances for broader social, ethical, or economic considerations. Realistically, this is very difficult to ascertain in those countries, such as the UK, where political influences are an integral part of the decision making process.

6.5 Independence of the Regulatory Decision-Making Process

6.5.1 The risk assessors

In Canada, Japan and the US, the risk assessments of biotech crops, and products derived from them, for environmental release and use in livestock feed or as human food are carried out by government scientists and professionals working within the respective regulatory authorities. This is also true for Australia's assessment of foods produced using gene technology. For Canada and the US, the incorporation of external scientific expertise, in the way of expert panels or committees, is not a general requirement for all risk assessments, but has nonetheless been accommodated on an *ad hoc* basis. Two recent examples include the CFIA consultations with the Bt Corn Coalition (1998) to establish mandatory insect resistance management plans, and a USDA/APHIS expert panel consultation on the risks associated with incorporating plant viral genes into transgenic plants (August 1997). This latter meeting was advertised in the US *Federal Register* and open to the public. As well, in the United States the requirements for public notification and comment periods provide another mechanism for regulatory officials to consider outside opinion.

Argentina, Australia and the UK have employed, either exclusively or in part, an approval system in which scientific advisory committees are responsible for evaluating applications and providing advice to Ministers. These committees may have statutory authority, in the case of CONABIA (Argentina) and ACRE (UK), or may be non-statutory as is the case for GMAC (Australia) and ACNFP (UK).

6.5.2 The decision makers

In some countries, the responsibility for product approval lies solely within the institutional structure of the regulatory authority. This is true for both Canada and the US, and is unlike the situation in other countries such as Australia and the UK. In the latter cases, the ultimate decision involves a visible political component, which in the case of the UK includes multinational (European Community) agreement.

6.6 The Role of Post-Market Surveillance

Fundamental to the Canadian regulatory framework for biotechnology products is the principle that products that have received regulatory approval are judged no more risky than comparable products with a history of safe use. This means, for example,

that an approved herbicide tolerant corn variety can be substituted for a traditional corn variety in agriculture without added risk to the environment and that the products derived from it can be used in livestock feed or human food without adversely affecting the health and/or nutritional status of the consumer. Philosophically then, post-market monitoring and long-term population health surveillance have not been judged necessary.

In line with this rationale, there are no regulatory requirements for additional segregation of commodities from PNTs or the labelling of novel foods, other than for health or safety-related reasons such as altered allergenic potential or significant changes to composition or nutritional quality. To date, there has been no organized post-market surveillance of these products in Canada.

Generally within the countries examined, the responsibility for post-market surveillance is covered by an ongoing duty of care on the part of the developer. The developer is expected to monitor for existing and emerging risks that may be associated with its product and notify the regulatory authorities whenever new information is uncovered. A recent example of this idea in action is the new information relating to glyphosate tolerant soybean (GTS 40-3-2) that was disclosed by Monsanto to regulatory authorities worldwide in May of this year. Monsanto had performed further characterization experiments on GTS 40-3-2 as part of a seed quality control program and to facilitate the development of detection methodologies. During the course of this work, Monsanto discovered that two additional partial nucleotide sequences corresponding to portions of the inserted 5-enolypyruvylshikimate-3-phosphate synthase gene were also incorporated into the plant genome. In each case, regulatory authorities that had previously approved this line of glyphosate tolerant soybean agreed that the additional non-functional sequences did not affect the overall safety of the product.

With the exception of the risk of selecting for resistant populations of insects because of the introduction of *Bt* crops, regulatory authorities have offered little if any guidance on monitoring parameters or sentinels for effective post-market surveillance.

The European Union, in its revised environmental release directive 90/220/EEC, is proposing that there be a statutory period of mandatory post-market monitoring. The period will be agreed at the point of giving commercial approval to the particular genetically engineered crop, and at the end of the review period a decision to renew the commercialization approval will be made based on any monitoring evidence.

There are currently no population based health surveillance programs linked to novel foods, or to any food for that matter, in any country. A key limitation is the lack of any system for monitoring the consumption patterns of novel foods in the population, and

health effects in both "exposed" and "non-exposed" individuals/populations, so that risk estimates can be derived.

7 Best Practices

Each of the countries reviewed here has taken a different approach toward the regulation of biotechnology and/or its products. Nowhere is this better illustrated than by comparing the US and the European Union, including the UK, who have approached this issue from entirely different perspectives. The US has adopted an optimistic mindset and approaches the evaluation of new products and technologies by questioning "Why not?", whereas, the European approach is more pessimistic and involves trying to predict the unknown and questioning "Why?". Not surprisingly, these differences in philosophy have been translated into unique regulatory systems with significant differences in intent (product vs process), legislative basis (existing vs technology specific laws), and location of decision-making authority (institutional vs political).

Notwithstanding the divergence of philosophical and/or political approach, at the scientific and technical level, each country asks very similar questions when evaluating the potential environmental and human health risks of biotechnology products. For example, in evaluating novel foods each country takes a comparative approach that focuses on the defined differences between the novel food and its traditional counterpart, and the effect these differences have on composition, nutritional quality, toxicology, and potential allergenicity. While it may not always be reflected in the regulatory decision making process, the rate of approvals, or the ultimate decision to allow marketing, there is a high degree of consistency in the scientific opinion in different countries about the safety of novel foods which have been put forward for commercialization to date.

In each country, the safety data upon which regulatory decisions are based are invariably produced or supplied by the developer without replication or direct verification by the regulatory authorities. Likewise, although there has been considerable debate on the merits of long term testing or population based health surveillance linked to genetically engineered foods, no country has yet designed or implemented such a system.

We believe that the following approaches or processes represent best practices in the regulation of agricultural biotechnology:

- **Canada's approach in which regulatory oversight is triggered solely by the novelty of traits expressed by plants or the novel attributes of foods or food ingredients.** Since it was first endorsed by the US National Academy of Sciences in 1987, the "product-based" approach to regulatory oversight has been validated by numerous scientific bodies and expert consultations. Canada's approach is unique and has been truest to the scientific principle that biotechnology is not inherently more risky than other technologies that have a long and accepted history of application in agriculture and food production. Even the US, which promotes its regulatory system as being "product-based", relies on the process of genetic engineering as a trigger for regulatory oversight of the environmental release of new plants or registration of plant-pesticides (*i.e.*, *Bt* toxin expressing crops).

  By way of example, there has been much debate in the popular press, and elsewhere, about the risks of creating "superweeds" because of natural outcrossing from herbicide tolerant canola varieties to weedy relatives and wild canola populations. There are commercial herbicide tolerant canola varieties that have been developed using both genetic engineering (glyphosate or glufosinate ammonium tolerant) and traditional plant breeding tools (imidazolinone or atrazine tolerant). The environmental impact of outcrossing from each of these varieties is the same. And yet, in every country besides Canada, the only herbicide tolerant varieties that are subject to environmental risk assessment or regulatory oversight are those produced through genetic engineering.

  However, Canada's approach makes the process of determining when a plant is in fact a "plant with a novel trait" more challenging and open to interpretation

The Validity of the "Product-Based" Approach

- "The potential occurrence of unintended effects is not unique to the application of recombinant DNA techniques but is also a general phenomenon in conventional breeding."—*Report of a Joint FAO/WHO Expert Consultation, May 29-June2, 2000, titled "Safety aspects of genetically modified foods of plant origin".*
- "I must emphasize that we believe it is the properties of a genetically modified plant, not the process by which it was produced, that should be the focus of risk assessments."—*Perry Adkisson, committee chair, US National Research Council committee on biotechnology*; and "No strict distinction exists between the health and environmental risks posed by plants genetically engineered through modern molecular techniques and those modified by conventional breeding practices."—*US National Research Council press release May 2000 following the report on "Genetically Modified Pest-Protected Plants: Science and Regulation".*
- "Risks associated with biotechnology-derived foods are not inherently different from the risks associated with conventional ones." and "There is no scientifically valid reason to treat possible gene transfer events involving GM organisms differently from those involving naturally occurring organisms. In any case, it is the gene and the trait it confers, and whether or not it brings a reproduction or selection advantage to the recipient organism that are crucial concerns when possible impacts of potential gene transfer are being considered."—*"Report of the task force for the safety of novel foods and feeds," OECD, May 17, 2000.*

than the simple test of whether it was produced using recombinant DNA technology.

- **The transparency of the regulatory decision making process as implemented in Australia and the United States.** In Australia, applications for environmental release (whether as field trials or general releases) and food safety evaluation are subject to two rounds of public notification and request for public comment prior to a final decision. The US requirement for notification in the *Federal Register* and solicitation of public comment in the case of petitions for deregulation by USDA-APHIS or registration as a plant-pesticide by EPA, fulfils a similar function.

  To date, only the Australia New Zealand Food Authority has implemented the practice of publishing draft risk assessments containing a detailed summary of the data submitted by developers as a proactive means of providing the general public with additional information upon which to base their comments or concerns. Recently the UK Food Standards Agency announced its intent to publicly release all of the information that developers supply to the Advisory Committee on Novel Foods and Processes, except material of a truly confidential nature. Similar initiatives by the US Food and Drug Administration to release submitted information and its conclusions with respect to industry consultations are encouraging.

  Greater transparency concerning both the risks and benefits of biotechnology products and how government decisions are made is an essential component of building public trust in new technologies. Broad disclosure is a stabilizing force not because the general public reads scientific studies or government decision documents, but because opinion leaders and those who intermediate information dissemination do.

- **The evidence-based approach to risk assessment that is free of consideration of social or ethical issues.** As a rule, risk assessments are fact-based evaluations of the likelihood of certain adverse outcomes, which by necessity are performed in the absence of perfect, or complete, information. They rely on the evidence available, not on the absence of evidence. Other approaches, such as the precautionary principle, tend to bias the process of "decision making under uncertainty" against the new and focus mainly on hazards, not risk. "Hazard" being the intrinsic potential of an agent to cause an adverse effect, whereas "risk" is the likelihood and magnitude of the adverse effect occurring under real world conditions. (*e.g.*, the transfer of antibiotic resistance marker genes from transgenic plants and their stable integration

into the genomes of bacteria in the human gut is a hazard, but the risk is insignificant).

In many respects, the regulatory world is a binary universe where decisions cannot be made in shades of grey. Evaluations of biotechnology products are conducted on a case-by-case basis, and are not amenable to a consideration of broader social or ethical issues in the process. These important issues need to be considered on a macro level that includes a public dialogue.

- **The performance of risk assessments by high-calibre credible scientists within the regulatory agencies.** A number of the countries examined in this comparison employ advisory committees (which are primarily, but not exclusively, scientific in nature) to evaluate the product safety information submitted by developers. Although this approach may seem an attractive alternative to using expertise within the regulatory authority, there are some drawbacks, including: committee members are part-time volunteers who cannot devote their full energies to risk assessments; out of necessity, committee meetings tend to occur only a few times per year, thus limiting efficiency; and the selection process for committee members may not result in the right combination of scientific expertise and regulatory experience.

  Although a complete exploration of the issue is beyond the scope of this document, product evaluations performed by competent scientists within the regulatory agency, supplemented by the use of issue-specific expert panel consultations as needed, may be the best approach.

  A critical factor is the breadth and depth of scientific expertise within the evaluator group. At the heart of the product evaluation process in every country is the scientific peer-review process, which has served as the basic mechanism for evaluating the veracity and significance of innovation in every area of scientific endeavour. The key phrase here is "peer review". Risk assessors for genetically engineered crops and novel foods must truly be peers of the academic or industrial scientists that developed these products.

It is encouraging to note that in Canada, the recent Federal Budget allocated nearly $9M to "*developing government technical capacity and human resources to address the increasing number of biotechnology products requiring regulation, conduct increasingly complex evaluations and ensure scientific parity with the industry it regulates*". This was part of a much larger allocation ($89.5M) for strengthening the regulatory system for biotechnology in Canada.

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