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Biosafety

The Safe Application of Biotechnology in Agriculture and the Environment

G.J. Persley, L.V. Giddings, and C. Juma

The World Bank / International Service for National Agricultural Research

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Executive Summary

The purpose of this document is to provide a practical guide for policymakers and research managers with limited time and restricted access to the extensive documentation that is accumulating on the safe use of biotechnology. It briefly reviews the development of modern biotechnology and provides guidance for policymakers who need to ensure that new biotechnology products are used safely within their countries.

Biosafety is one term that is used to describe the policies and procedures adopted to ensure the environmentally safe application of modern biotechnology. It is a term that is gaining wider currency as more countries seek to benefit from the application of modern science in medicine, agriculture, and the environment, without endangering public health or environmental safety.

This document suggests a series of steps that might be taken to establish a national biosafety system. As a first step, a national biosafety committee should be established. The national committee should then move quickly to establish policies and procedures to govern the use of modern biotechnology in the country. These should govern both in-country research and the import and sale of new biotechnological products from elsewhere. The national committee should also oversee the establishment of biosafety committees in those institutions undertaking advanced biological research in the country. Each of these institutions should also have a designated biological safety officer.

This document recommends that a national biosafety system should be established within the existing regulatory framework and draw on existing institutions, personnel, and current legislation to the greatest extent possible. It recommends that the focus in the regulatory process should be on the nature of the product itself, not on the techniques used to produce it. It also provides an annotated bibliography and a list of institutions and individuals from whom more detailed information and advice can be sought.

In the 1970s, the power of the new techniques in modern biology led scientists to exercise caution in their use in order to avoid any inadvertent introduction of harmful effects. Considerable experience has now accumulated on the use of the new genetic techniques in the laboratory, in small-scale field trials for agricultural

purposes, and for commercial purposes, especially in medicine but also increasingly in agriculture. This is leading to the establishment of better-defined regulatory practices in many countries.

Similar patterns of regulation are evolving for both contained and uncontained applications of biotechnology: initial stringency and caution, followed by less stringent regulatory requirements as experience accumulates on the use of new products from modern biotechnology.

In agriculture and medicine, several new diagnostic products and vaccines have been released commercially. New biological control agents devised by the use of recombinant-DNA technology have also been released commercially. Over 400 small-scale field trials of potentially useful plant varieties, developed with the use of genetic engineering, have been conducted in some 20 countries. The most promising material from these trials is being carried forward for release as new varieties of crop species in several countries. The first such releases of new plant varieties resulting from genetic engineering are expected within the next two years (e.g., cotton, potatoes, tomatoes).

All these applications of modern biotechnology are being developed under safeguards for good laboratory practices and recombinant-DNA safety considerations, as described by the Organization for Economic Cooperation and Development (OECD) in 1986 for laboratory-based experimentation and extended in 1992 to guidelines for small-scale field trials. The OECD guidelines have been used as the basis for national guidelines in many countries. They remain the most authoritative set of internationally agreed-upon guidelines presently available and provide a sound basis for national policymakers in all countries.

The OECD guidelines have been complemented by several authoritative studies that have developed risk-assessment procedures appropriate for guiding the release of biotechnology products. They provide steps for determining instances of low, medium, and high risk, largely based on the degree of familiarity with similar procedures and products.

There are several initiatives in progress aimed at the international harmonization of biosafety approaches at a global or regional level. In July 1991 the UNIDO Secretariat prepared a voluntary code of conduct for the release of organisms into the environment on behalf of the UNIDO/UNEP/WHO/FAO working group on biosafety. This document should prove useful to many countries. In Latin America, the Instituto Interamericano de Cooperación para la Agricultura (IICA) has prepared guidelines for the experimental use of genetically modified organisms and their

release into the environment. These are providing the basis for a common, regional approach to biosafety in the countries of the Andean cone of Latin America.

This brief has been prepared primarily for national policymakers and research managers. It may also make a contribution to discussions on the environmentally sound management of biotechnology that are taking place in the context of the United Nations Conference on the Environment and Development (UNCED) held in Brazil in 1992.

In summary, five key principles relevant to the preparation of national policies and procedures for the regulation of biotechnology are

1. Regulatory review should focus on the characteristics and identified risks of the biotechnology product, not the process by which it is created.

2. For those biotechnology products that require review, the review process should be designed for efficiency and effectiveness while assuring the protection of public health and environmental safety.

3. Regulatory requirements for modern biotechnology should be integrated into the overall regulatory system which governs the release of new products in the agricultural sector.

4. The degree of familiarity with the behavior of similar organisms when released into the environment should determine the level of regulatory oversight required. This may range from minimal to extensive, depending on the degree of hazard identified.

5. Regulatory programs should be flexible and capable of adapting quickly to the new knowledge and understanding produced by the rapid advances in biotechnology.

Introduction

The purpose of this document is to review the development of modern biotechnology and provide guidance for policymakers and research managers who need to ensure that new biotechnology products are used safely in their country.

It is divided into four sections. The first section describes the overall context for modern biotechnologies. The second summarizes the broader themes of risk assessment and management, as well as safety regulation by governments, as distilled from existing authoritative studies. The third provides specific suggestions for policies and procedures that national authorities may wish to consider in establishing a biosafety system tailored to their specific requirements. The fourth section summarizes the various international activities that are in progress to foster the international harmonization of approaches to biosafety. Supplementary information is contained in the appendices.

The constitution of a national biosafety system is important both to foster the development of modern biotechnology within a country and to ensure access to modern biotechnology products generated elsewhere. The absence of a suitable regulatory framework for biotechnology makes it difficult for development agencies and private companies not only to invest in biotechnology in a particular country, but also to make the products of biotechnology available in that country. Thus, a safe and efficient regulatory process is in itself a comparative advantage in biotechnology and a prerequisite for access to technology in this rapidly expanding field.

Setting the Context

Biotechnology refers to any technique that *uses living organisms or substances from those organisms to make or modify a product, to improve plants or animals, or to develop microorganisms for specific uses.*

Biotechnology consists of a gradient of technologies, ranging from the long-established and widely used techniques of **traditional biotechnology** (e.g., food fermentation, biological control) through to **modern biotechnology**,

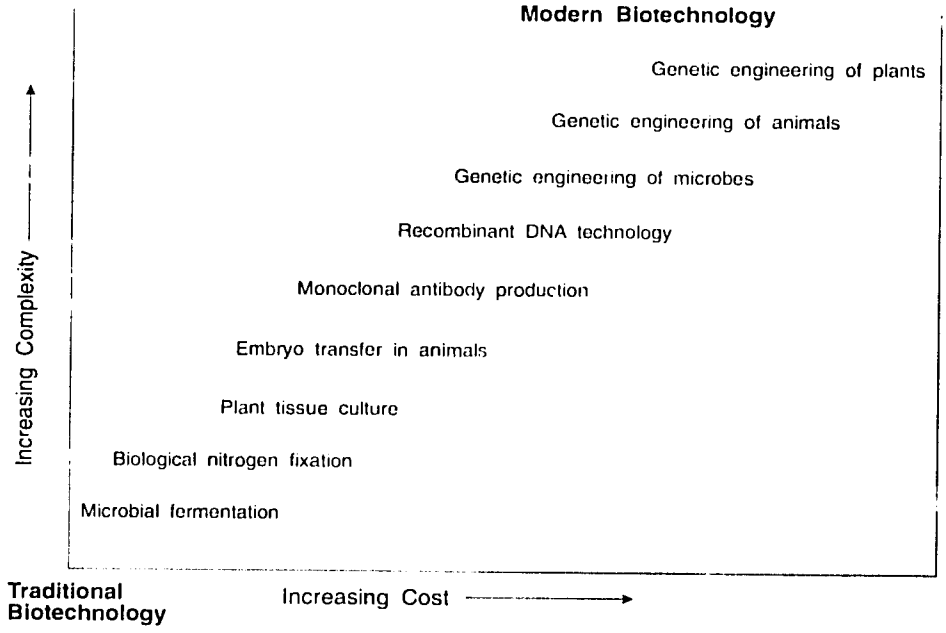
which is based on the use of new techniques of recombinant-DNA technology (often called *genetic engineering*), monoclonal antibodies, and new cell- and tissue-culture methods (figure 1).

Biotechnology is not a new science; rather, it is a new term that has been given to the recent evolution of the science of genetics. This science originated in the late nineteenth century with the pioneering work of Gregor Mendel.

During the 1970s scientists developed new methods for combining portions of DNA (deoxyribonucleic acid, the biochemical material in all living cells that conveys the instructions that govern hereditary characteristics) and for moving portions of DNA from one organism to another. This set of enabling techniques is referred to as *recombinant-DNA technology* or *genetic engineering*.

Over the past two decades there has been an exponential increase in the number of significant advances in genetics (figure 2). It is this increase in new techniques for understanding and modifying the genetics of living organisms that has led to the greatly increased interest and investments in biotechnology over the past two decades.

The principal effect of the new techniques of modern biotechnology in agriculture is to broaden the range of hereditary material that can be utilized by conventional breeding programs in the production of new varieties of useful



Source: Persley (1990).

Figure 1. Gradient of biotechnologies

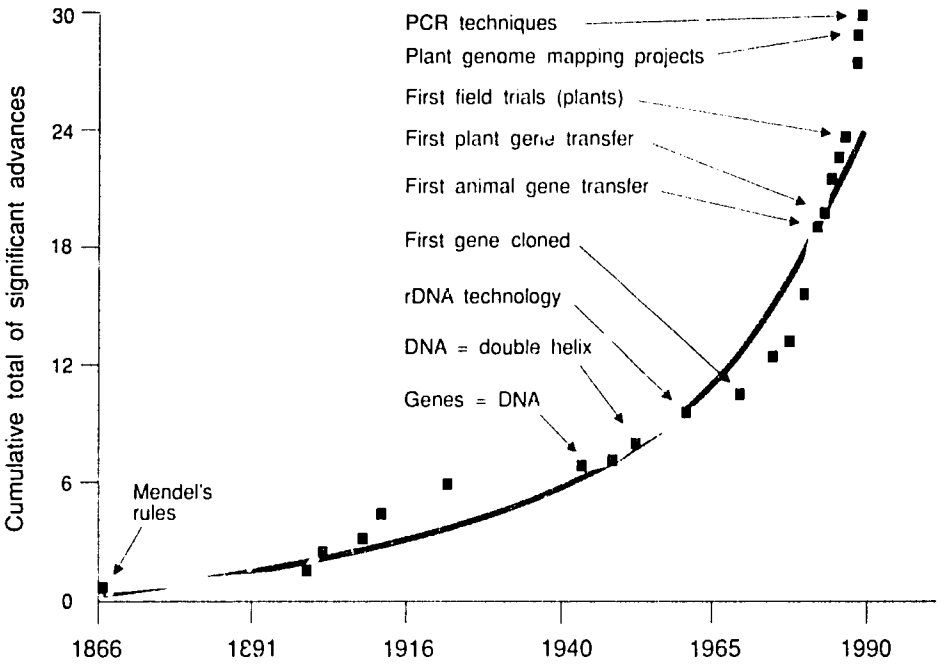


Figure 2. Biotechnology milestones, 1866–1992

plants, animals, and microbes. The applications developed from these new methods place them firmly within the continuum of techniques used in industry, agriculture, and food processing throughout human history. Thus, while modern biotechnology provides powerful new tools, these tools are used to generate products that fill essentially the same roles as those produced with more traditional methods. The properties of these products do not differ substantially from those with which we are already familiar.

The most striking differences between the techniques of modern biotechnology and those that have been used for many years lie in the increased precision with which the former may be used, and the shorter time required to produce results. For example, to transfer a trait from one crop variety to another by conventional plant breeding requires the crossing (hybridization) of two different varieties. This exchange of genetic material involves transferring not only the gene controlling the trait of interest, but also about half of all the genes from the variety carrying this trait. This, in turn, makes necessary a long and laborious process of backcrossing to eliminate as much unwanted genetic material as possible. Using conventional breeding techniques, undesirable characteristics are often transmitted along with the trait of interest, and most of the time and effort in a conventional breeding program is consumed in identifying and eliminating such undesirable traits.

Modern recombinant-DNA technology (*genetic engineering*), enables plant

breeders to collaborate with molecular biologists to transfer to a popular and highly developed crop variety only the one or two genes needed to impart a new characteristic, such as a specific kind of pest resistance. This much more precise method of genetic transfer eliminates the need for time-consuming and difficult backcrossing. It can reduce the total development time and cost for a new variety substantially. This increased precision in plant and animal breeding translates into improved predictability of the resulting products. Improved predictability, in turn, means greater safety. In addition, the products of modern biotechnology must go through extensive trials for yield, agronomic characteristics, and quality at different sites and over a number of seasons, in the same manner as the products of conventional breeding programs are evaluated.

Concerns have been raised about the new techniques of modern biotechnology because their potential power is so far-reaching, and the number of new products so great. **It is important to provide appropriate regulatory mechanisms to ensure that products produced by the use of new techniques are as safe as the products of traditional biotechnology.**

Implications for Biosafety

Biotechnology Products

The products of modern biotechnology in agriculture are used in the environment and for human consumption. Here, the characteristics of the products themselves determine their safety. The processes used to generate the products are relevant only insofar as they describe product qualities or characteristics. This principle has been reiterated in several extensive studies which have examined the implications of the use of modern biotechnologies in medicine, agriculture, and the environment (e.g., NRC 1989; OECD 1986, 1990, 1991, 1992; OTA 1988; Tiedje et al. 1989).

The products of modern biotechnology in agriculture include plants, animals, and microbes with, for example, increased resistance to diseases or pests, altered nutritional requirements, or modified performance characteristics. Some have expressed concern that these products require special scrutiny because of the means used to produce them. This is necessary, it is argued, because of the difficulty in predicting their behavior, particularly when they are released into the environment. Several of the studies listed above have examined these questions and have concluded that **the characteristics of mod-**

ern biotechnology products that have already been produced, are now under development, or are anticipated are generally similar to those produced with traditional techniques, and are consequently familiar to regulatory authorities (e.g., NRC 1989; OECD 1991).

Modern biotechnology products are derived primarily from materials with which we have long experience in agriculture, industry, and commerce. Furthermore, given the challenges in producing genetically engineered organisms that will survive in the environment long enough to perform the desired functions, researchers have a powerful incentive to work with well-characterized systems and organisms as much as possible.

The evolution of regulatory policies in countries that have accrued the most experience with biotechnology products demonstrates a pattern of initial stringency and caution followed by less stringent regulatory requirements as reassuring experience accumulates. This has been the case with the US National Institutes of Health guidelines, which are widely used for laboratory-based research with recombinant DNA. Procedures for assessing and managing the risks of biotechnology products intended for uncontained use began with a similarly cautious approach. In the US, over 400 small-scale field tests have been conducted, which include a range of plant species (e.g., cotton, maize, potatoes, rapeseed, rice, tomatoes, and soybeans) and microorganisms. In light of the experience gained in these trials, procedures are being developed to govern large-scale releases of genetically engineered organisms for commercial use in agriculture. In addition, regulatory processes are being reviewed to increase their efficiency and to provide a better link between the degree of regulation required and a demonstrable degree of hazard (US President's Council on Competitiveness 1991; US Office of Science and Technology Policy 1992).

Risk Assessment

Tiedje et al. (1989), in their study for the Ecological Society of America, present a list of important criteria to consider regarding the safety of planned introductions. They also develop risk-assessment criteria established in Australia and shows how such criteria might be linked together in a flexible review scheme that should be of great interest and value to regulators (Millis 1990).

The US National Academy of Science (NAS) and its National Research Council (NRC) have released a report on establishing a framework for decisions on the introduction of genetically modified microorganisms and plants into the environment (NRC 1989). The study was

charged with identifying criteria for defining risk categories and recommending ways to assess the potential risks associated with introducing modified organisms into the environment.

The report reiterates the principle of the earlier document that **safety assessment of a recombinant-DNA-modified organism "should be based on the nature of the organism and the environment into which it will be introduced, not on the method by which it was modified"** (NAS 1987). It also points out that although genetic modification by molecular methods may be more powerful and capable of producing a wider range of phenotypes, **"no conceptual distinction exists between genetic modification of plants and microorganisms by classical methods or by molecular methods that modify DNA and transfer genes"** (NAS 1987).

The NRC also recognizes that there is a long history of utility and safety in the use of plants and microorganisms. **"Society has benefitted greatly from the use of genetically modified microorganisms and plants, and field testing is essential to increase our knowledge about the relative safety or risk of large-scale use of genetically modified organisms and to determine the potential utility of the modified organisms"** (NRC 1989).

With regard to the **field-testing of genetically modified plants**, the NRC report concludes that

1. Plants modified by classical genetic methods are judged safe for field testing on the basis of experience with hundreds of millions of genotypes field-tested over decades. The current means for making decisions about the introductions of classically bred plants are entirely appropriate and no additional oversight is needed or suggested.

2. Crops modified by molecular and cellular methods should pose risks no different from those modified by classical genetic methods for similar traits. As the molecular methods are more specific, users of these methods will be more certain about the traits they introduce into the plants. Traits that are unfamiliar in the specific plant will require careful evaluation in small-scale field tests where plants exhibiting undesirable phenotypes can be destroyed.

3. The potential for enhanced weediness is the major environmental risk perceived for introductions of genetically modified plants. The likelihood of enhanced weediness is low for genetically modified, highly domesticated crop plants, on the basis of our knowledge of their morphology, reproductive systems, growth requirements, and unsuitability for self-perpetuation without human intervention.

4. Confinement is the primary condition for ensuring the safety of field introductions of classically modified plants.

5. Depending on the crop species, proven confinement options include

biological, chemical, physical, spatial, environmental, and temporal isolation, as well as size of field plot.

6. Plants grown in field confinement for experimental purposes rarely, if ever, escape to cause problems in the natural ecosystem.

7. Established confinement options are as applicable to field introductions of plants modified by molecular and cellular methods as they are to introductions of plants modified by classical genetic methods.

With regard to the **field testing of genetically modified microorganisms,** the NRC report concludes that

1. The precision of many molecular methods allows scientists to make genetic modifications in microbial strains that can be fully characterized, in some cases to the determination of specific alterations of bases in the DNA nucleotide sequence.

2. The molecular methods have great power because they enable scientists to isolate genes and to transfer them across biological barriers.

3. Although field experience provides considerable information about some microorganisms (e.g., rhizobia, mycorrhizae, and many plant pathogens and biocontrol agents), information regarding the ecology of microorganisms and experience with planned environmental introductions of genetically modified microorganisms is limited compared with that regarding plants. No adverse effects have developed from introductions of genetically modified microorganisms to date. Ecological uncertainties can be addressed scientifically regarding the genetic and phenotypic characteristics of microorganisms as well as by considering environmental attributes such as nutrient availability.

4. The likelihood of possible adverse effects can be minimized or eliminated by appropriate measures to confine the introduced microorganism to the target environment, for example, by introducing "suicide" genes, as they become practicable, into the organisms.

The NRC report also provides frameworks for the evaluation of risk for the release of plants and microorganisms. These frameworks are based on the following criteria:

1. Are we familiar with the properties of the organism and the environment into which it may be introduced?

2. Can we confine or control the organism effectively?

3. What are the probable effects on the environment should the introduced organism or a genetic trait persist longer than intended or spread to nontarget environments?

When the familiarity standard for a plant or microorganism has been satisfied such that there is reasonable assurance that the organism and the other

conditions of an introduction are essentially similar to known introductions, and when these have proven to present negligible risk, the introduction is assumed to be suitable for field testing according to established practice.

The familiarity criterion is central to the suggested evaluation framework. It permits decision makers to draw on past experience introducing plants and microorganisms into the environment, and it provides flexibility. As field tests are performed, information will continue to accumulate about the organisms, their phenotypic expression and their interactions with the environment. Eventually, entire classes of introductions may become familiar enough to require minimal oversight.

***Familiar* does not necessarily mean safe. Rather, to be familiar with the elements of an introduction means to have enough information to be able to judge its safety or risk.**

When knowledge of the type of modification, the species being modified, or the target environment is insufficient to meet the familiarity criterion, the proposed introduction must be evaluated according to whether the organism can be confined or controlled, as well as the potential effects of a failure to confine or control it — which define the relative safety or risk of the introduction.

An NRC-recommended framework to assess field testing of genetically modified plants and microorganisms and determine the degree of familiarity of a particular case is shown in appendix D.

Regulators may therefore use the criterion of familiarity as a guide: How familiar are we with products of this type? How familiar are we with the starting materials? How familiar is the behavior of similar products in the environment for which it is intended? If the level of familiarity is high, then the product can be reviewed within existing regulatory or safety assurance systems. As areas of increasing unfamiliarity emerge, appropriate adaptations to existing review procedures may become necessary.

The possible types of risks to be assessed in agricultural biotechnology are the likelihood of the product showing characteristics of

- potential for the plants to become weeds;
- likely toxicity of plants and plant materials;
- potential pathogenicity of microorganisms;
- potential for animals to become pests.

These risks are similar to those assessed when an exotic plant, animal, or microorganism is to be introduced into any area, often for the purpose of biological control of a pest. In many instances in the use of modern biotechnology, we will be much more *familiar* with the likely behavior of the genetically modified organism, if it is based on a single-gene modification of its parent, than if it were an exotic organism with which we are *unfamiliar* in this environment.

It follows that, if problems arise in conjunction with the use of modern biotechnology products, they are most likely to be similar to problems with which we are already familiar and experienced as a result of using traditionally generated products in similar settings (NRC 1989).

In evaluating the potential risks associated with these new technologies, the appropriate question is not "How can we reduce the potential risks to zero?" but "What are the relative risks of the new technologies compared with the risks of the technologies with which they will compete? . . . What are the risks posed by overregulating or failing to fully develop new technologies? How do we weigh costs and benefits?"

It would be unfortunate if concerns over the potential impact of planned introductions of genetically engineered organisms, which may be safer than the competing chemical technologies they could displace, lead to such a stringent and expensive regulatory approach that economics force continued reliance on older, less safe technologies, such as the widespread use of chemical pesticides in the environment.

Possible National or Regional Biosafety Systems

The approach a country takes to ensure the safety of modern biotechnology products will depend on the regulatory structures in place. Five principles that merit consideration by national policymakers are listed below:

1. Regulatory review should focus on the characteristics and risks of the biotechnology product — not the process by which it is created.

2. For biotechnology products requiring review, the review process should be set up for efficiency and effectiveness while assuring the protection of public health and environmental safety.

3. Any additional regulatory requirements for new biotechnology products should be integrated into the overall regulatory systems that govern the release of new products in the agricultural sector.

4. Regulatory programs should be flexible and capable of adapting quickly to new knowledge and understanding produced by the rapid advances in biotechnology.

5. To create opportunities for the application of innovative biotechnology products, all regulation in environmental and health areas — whether or not they address biotechnology — should use performance standards rather than rigid controls or specific design requirements.

Biosafety Guidelines

There are advantages in incorporating biotechnology regulation in existing legislation and institutional arrangements to avoid creating a new regulatory infrastructure specifically for biotechnology. New guidelines, linked with relevant existing legislation, can be formulated and implemented to cover laboratory practices, small-scale field trials, and commercial releases. This usually requires establishing a national biosafety committee, supported by an institutional biosafety committee in each research institute dealing with modern biotechnology.

Based on the following, Millis (1990) described the advantages of this approach to the development of biosafety guidelines:

- Flexible guidelines that can readily be amended in response to new techniques.

- Practicing scientists (e.g., molecular biologists, microbiologists, epidemiologists, ecologists) can serve on the assessment committees on a part-time basis, thus ensuring that current expertise is always available.

- Laws always lag behind events, and in this area of science, the expansion of knowledge is rapid.

- Laws are designed to be interpreted precisely; guidelines set out the spirit of the restraints as well as detailed requirements.

- Guidelines are acceptable in a court of law in judging whether an action is dangerous or negligent.

- Employers have legal responsibility for their employees, and employers can require employees to abide by the guidelines.

- Government employment, research supported by government money, and all tax or other concessions granted by government to industry can be made conditional upon the beneficiary abiding by the guidelines.

- In most countries there is legislation (in addition to common-law provisions) that could control new technology. New legislation may duplicate existing regulations and, at worst, cause conflicts between different regulating bodies.

- The hazards of genetic manipulation are still conjectural and, hence, guidelines seem more appropriate than laws, which are generally designed to address a specific, defined problem.

National Biosafety Committee

The first step in developing appropriate policies and procedures for the regulation of biotechnology is to establish a national biosafety advisory committee. Possible terms of reference for such a committee are given in table 1. The purpose of the national committee is to set policy and procedures at the national level and to provide technical advice to the regulatory authorities and the institutions responsible for the development of biotechnology in the country.

The national biosafety committee may be a subcommittee of a national biotechnology committee, where one exists. It should contain members with a range of relevant scientific disciplines (e.g., microbiologist, geneticist, ecologist) in addition to nontechnical members representative of community interests.

The situations a national biosafety committee is likely to have to deal with are

- assessment and regulation of in-country research;
- assessment of safety of imported biotechnology products.

For in-country research, this requires that the national biosafety committee set out required guidelines for laboratory and field research and establish the necessary structures and responsibilities to see that these are implemented by the relevant organizations in the country.

An important consideration in dealing with requests for permission to field-test or market modern biotechnology products for commercial applications is to determine whether existing safety-assurance mechanisms are adequate to evaluate biotechnology (or other new) products. These issues are best considered by governments well in advance of receiving requests for permission to test or market new products in order to avoid regulatory uncertainty or undue delay in considering the potential applications of biotechnology in the country.

If there are appropriate regulations and procedures in-country that govern the release of new plant varieties, the sale of vaccines and pesticides, and the release of biocontrol agents, these same mechanisms can be used to regulate the use of the products of modern biotechnology. If not, then appropriate legislation and regulations need to be introduced in order to have a suitable regulatory framework for the agriculture sector as a whole.

Table 1. Suggested Terms of Reference for a National Biosafety Committee (NBC)

Having regard to the Government's wish for a *system for technical and biosafety* advice to be provided to the Ministers and other appropriate governmental authorities on the continuing assessment of the risks and benefits, associated with the production and/or application of biological materials produced in laboratories and which occur in nature, *the Committee shall:*

1. Establish and review, as necessary, Guidelines for both physical and biological containment and/or control procedures appropriate to the level of assessed risk involved in relevant research, development and application activities.
2. Review relevant proposals, except those that relate to research under contained laboratory conditions, and recommend any conditions under which this work should be carried out, or that the work not be undertaken.
3. Consult with relevant government agencies and other organizations as appropriate.
4. Report to the Minister and other responsible governmental authorities at least annually, and also report promptly after any breaches of the Guidelines referred to in 1 above, and on other relevant matters referred to them.
5. Establish contact and maintain liaison with such monitoring bodies in other countries and with international organizations, as is appropriate.
6. As necessary, advise on the training of personnel with regard to safety procedures.
7. Collect and disseminate information relevant to the above, having due regard to the special circumstance relating to proprietary information.
8. Establish and oversee the work of a scientific subcommittee, whose guidelines follow and whose role and function include not only participation in items 3, 5, 6, 7, above, but also all research performed under contained laboratory conditions.

The Scientific Subcommittee shall:

1. Be formed to support the work of the NBC. It shall enter into discussions directly with scientists and institutions where they work, and with fund-granting bodies in determining the conditions under which research should be carried out.
2. Review proposals for such research and recommend any conditions under which experiments should be carried out, or that work not be undertaken.
3. Provide technical advice to the NBC and contribute to its functions in relation to laboratory contained research.

Sources: Adapted from IICA (1988) and Millis (1990).

For imported biotechnology products, the regulatory responsibility should rest with the relevant regulatory agency that monitors the importation of biological agents into the country (e.g., the animal and plant quarantine service). The national biosafety committee should play an active advisory role to this agency to assist in assessing the adequacy of the tests done in the product's country of origin and determining if there is a need for any further local testing of the product prior to its commercial use. In these assessments, the national committee may wish to draw on expert advice from outside the country from those familiar with the characteristics and behavior of the product in its country of origin. A list of possible sources of additional information and advice for the assessment of specific cases is given in appendix A.

Institutional Biosafety Committees

The National Biosafety Committee should request that each institution in the country conducting research in modern biotechnology establish an institutional biosafety committee (IBC) and designate a biological safety officer.

Table 2 gives terms of reference for an institutional biosafety committee. The responsibilities of a biological safety officer are described in table 3.

The IBC's terms of reference and a list of its members and their qualifications should be widely circulated within the institution and to the national committee, as well as made publicly available.

The membership of an institutional biosafety committee should include members with the appropriate technical expertise as well as external experts and lay members. The IBC should have enough scientific expertise so that it is not totally dependent on the advice of a project supervisor to make assessments of that supervisor's projects. The institute may also wish to consider the inclusion of persons with a broader background — one not necessarily technical — on the committee. In addition, the national biosafety committee may consider it desirable to appoint some persons from outside the organization to the IBC.

It is recognized that some organizations, particularly smaller ones, may have difficulties setting up an institutional biosafety committee with the requisite breadth of expertise. In such cases, the national biosafety committee could provide the necessary advice and assistance to fulfill the role of the IBC for the institution. Alternatively, it could arrange for several smaller organizations to constitute a common institutional biosafety committee.

Table 2. Suggested Terms of Reference for an Institutional Biosafety Committee (IBC)

1. To review and endorse applications;
2. To consult with and request approvals from the National Biosafety Committee (NBC);
3. To implement the recommendations of the NBC;
4. To establish a program of inspections to ensure that the physical containment facilities continue to meet requirements and that the other procedures and practices specified in these guidelines are followed;
5. To ensure that all personnel involved in the work have sufficient training and experience;
6. To maintain a list of project supervisors and other supervisors approved by the IBC as competent to perform supervisory duties for particular projects;
7. To maintain individual records and files of individual research projects;
8. To investigate and report promptly to the NBC all accidents, unexplained absences and illnesses;
9. To provide an annual report to the NBC.

Table 3. Suggested Terms of Reference for a Biological Safety Officer (BSO)

1. The officer should be familiar with the biosafety requirements for the recombinant -DNA work and facilities, and be able to make checks and advise on biosafety issues on a day-to-day basis.
2. The officer should be given sufficient independence and authority to ensure that biosafety is not compromised by other considerations.
3. The officer may be a member of the Institutional Biosafety Committee (IBC).
4. A report from the officer should form part of the IBC's annual report to the National Biosafety Committee.

Source: Adapted from IICA (1988).

Project Supervisors

For each project concerned with modern biotechnology, there should be a designated project supervisor responsible for all aspects of the work. This

person should take full responsibility for accurately and completely describing the proposed project to the IBC and for carrying out the work in accordance with this description. The project supervisor must also ensure that all workers are suitably trained for the tasks they will perform, as well as in safety and emergency procedures, for which clear protocols must exist. Workers must be familiar with any hazards in the work area and be informed of the purpose of these guidelines.

The project supervisor, and indeed all persons who will at some time supervise the work, must be approved by the IBC as having the requisite competence. The IBC should maintain a list of approved supervisors. If the project supervisor is changed, the IBC should be advised promptly.

International Harmonization

International harmonization of biosafety guidelines is the subject of discussion in several fora, primarily in the OECD and several UN agencies.

European Community (EC)

The EEC Council released directives in April 1990 on the contained use and deliberate release into the environment of genetically modified organisms. These were to be implemented by October 1991 by all member countries. However, several countries have encountered difficulties in interpreting and implementing these directives into national law.

Organization for Economic Cooperation and Development (OECD)

The Organization for Economic Cooperation and Development (OECD) has sponsored continuing collaboration among its member countries on safety

in biotechnology since the early 1980s. It prepares guidance documents that are broadly accepted by all OECD member countries, and which are often used in shaping national policies and guidelines in many OECD member countries. Two principal publications have been prepared by an OECD committee of national experts from 25 countries. The first is the 1986 study on *Recombinant DNA Safety Considerations* (OECD 1986). It contained recommendations on safety considerations on the applications of recombinant-DNA organisms in industry, agriculture, and the environment which were endorsed by the OECD Council (table 4). The OECD guidelines are the best intergovernmentally agreed-upon guidelines presently available. **They are recommended as a basis for the development of national policies and procedures.**

The second document is a 1992 publication that provides updated safety criteria and guidelines for "good industrial large-scale practice" for the handling of low-risk recombinant-DNA microorganisms in industrial production (OECD 1992). It also describes good development principles for the design of safe, small-scale field trials with genetically modified plants and microorganisms, endorsed by the OECD. The OECD is presently considering similar guidelines for large-scale field trials of genetically modified plants and microorganisms.

Intended to be scientifically based, the OECD documents have the broadest support of any of intergovernmental or international documents. They are recommended as guides for developing national policies and procedures.

UNIDO/UNEP/WHO/FAO Working Group on Biosafety

An informal working group of representatives from four UN agencies has been reviewing biosafety issues over the past several years. On behalf of the working group, the UNIDO Secretariat has prepared a voluntary international code of conduct for release of organisms into the environment. A group of internationally recognized experts from several countries met twice in 1990-91 to prepare the voluntary code of conduct. This document outlines general principles or standards of practice applicable to the introduction of organisms or their products/metabolites into the environment. It sets out basic guidelines for both governments and scientists. The guidelines are framed to encourage the commercial use of biotechnology products. This document should be valuable to those seeking to place biotechnology products and their risks and benefits in an appropriate perspective. It provides an international perspective from which to develop further national policies and procedures.

Table 4. Recommendations of OECD's Council Concerning Safety Considerations for Applications of Recombinant-DNA Organisms in Industry, Agriculture, and the Environment

The Council,

Considering that recombinant-DNA techniques have opened up new and promising possibilities in a wide range of applications and can be expected to bring considerable benefits to mankind:

- Recognizing, in particular, the contribution of these techniques to improvement of human health and that the extent of this contribution is expected to increase significantly in the near future;
- Considering that a common understanding of the safety issues raised by recombinant-DNA techniques will provide the basis for taking initial steps towards international consensus, the protection of health and the environment, the promotion of international commerce and the reduction of national barriers to trade in the field of biotechnology;
- Considering that the vast majority of large-scale, industrial, recombinant-DNA applications will use organisms of intrinsically low risk that warrant only minimal containment consistent with good industrial large-scale practice (GILSP);
- Considering that the technology of physical containment is well known to industry and has successfully been used to contain pathogenic organisms for many years;
- Recognizing that, when it is necessary to use recombinant-DNA organisms of higher risk, additional criteria for risk assessment can be identified and that these organisms can also be handled safely under appropriate physical and/or biological containment;
- Considering the assessment of potential risks of recombinant-DNA organisms for environmental or agricultural applications is less developed than the assessment of potential risks for industrial applications;
- Recognizing the assessment of potential risk to the environment of environmental and agricultural applications of recombinant-DNA organisms should be approached with reference to, and in accordance with, information held in the existing data base, gained from the extensive use of traditionally modified organisms in agriculture and the environment generally, and that with step-by-step assessment during the research and development process potential risk should be minimized;
- Considering the present state of scientific knowledge;
- Recognizing that the development of general international guidelines governing agricultural and environmental applications of recombinant-DNA organisms is considered premature at this time;

Table 4. (continued)

- Recognizing that there is no scientific basis for specific legislation to regulate the use of recombinant-DNA organisms;

On the proposal of the Committee for Scientific and Technological Policy:

1. RECOMMENDS that Member countries
   a. share, as freely as possible, information on principles or guidelines for national regulations, on developments in risk analysis and on practical experience in risk management with a view to facilitating harmonization of approaches to recombinant-DNA techniques;
   b. examine their existing oversight and review mechanisms to ensure that adequate review and control of the implementation of recombinant-DNA techniques and applications can be achieved while avoiding any undue burdens that may hamper technological developments in this field;
   c. recognize, when aiming at international harmonization, that any approach to implementing guidelines should not impede future developments in recombinant-DNA techniques;
   d. examine at both national and international levels further developments such as testing methods, equipment design and knowledge of microbial taxonomy to facilitate data exchange and minimize trade barriers between countries. Due account should be taken of ongoing work on standards within international organizations, e.g., WHO, CEC, ISO, FAO, MSDN;[a]
   e. make special efforts to improve public understanding of the various aspects of recombinant-DNA techniques;
   f. watch the development of recombinant DNA techniques for applications in industry, agriculture, and the environment, while recognizing that for certain industrial applications, and for environmental and agricultural applications of recombinant DNA organisms, some countries may wish to have a notification scheme;
   g. ensure the assessment and review procedures protect intellectual property and confidentiality interests in applications of recombinant DNA, recognizing the need for innovation while still ensuring that all necessary information is made available to assess safety.
2. RECOMMENDS, with specific reference to industrial applications, the Member countries:
   a. ensure, in large-scale industrial applications of recombinant DNA techniques, that organisms which are of intrinsically low risk are used wherever possible, and handled under the conditions of Good Industrial Large-Scale Practice (GILSP) described in the report;

Table 4. (continued)

b. ensure that, when a risk assessment using the criteria defined in the report indicates that a recombinant DNA organism cannot be handled merely by GILSP, appropriate containment measures, in addition to GILSP, and corresponding to the risk assessment are applied;

c. encourage, in large-scale industrial applications requiring physical containment, further research to improve techniques for monitoring and controlling nonintentional release of recombinant-DNA organisms.

3. RECOMMENDS, with specific reference to agricultural and environmental applications, that Member countries

a. use the existing considerable data on the environmental and human health effects of living organisms to guide risk assessments;

b. ensure that recombinant-DNA organisms are evaluated for potential risk, prior to applications in agriculture and the environment by means of an independent review of potential risks on a case-by-case[b] basis;

c. conduct the development of recombinant-DNA organisms for agricultural or environmental applications in a stepwise fashion, moving, where appropriate, from the laboratory to the growth chamber and greenhouse, to limited field testing and finally, to large-scale field testing;

d. encourage further research to improve the prediction, evaluation, and monitoring of the outcome of applications of recombinant-DNA organisms.

4. INSTRUCTS the Committee for Scientific and Technological Policy to:

a. review the experience of Member countries in implementing the principles contained in the report;

b. review actions taken by Member countries in pursuance of the Recommendation and to report thereon to the Council;

c. consult with other appropriate Committees of the OECD in developing proposals for a coordinated future work program in biotechnology.

Source: OECD (1986).

a. WHO = World Health Organization, CEC = Commission of the European Communities, ISO = International Standards Organization, FAO = Food and Agriculture Organization of the United Nations. MSDN = Microbial Strains Data Network.

b. Case-by-case means an individual review of each proposal against assessment criteria that are relevant to that particular proposal. This is not intended to imply that every case will require review by a national or other authority since various classes of proposals may be excluded.

United Nations Conference on the Environment and Development (UNCED)

The environmentally sound management of biotechnology is one of the priority areas being examined in relation to UNCED. A series of initiatives are being proposed in a document entitled "Agenda 21," to be considered at the UNCED conference in Brazil in June 1992. Five program areas are proposed: (1) increasing the availability of food, fuel, and renewable raw materials; (2) improving human health; (3) protecting the environment; (4) improving safety and international cooperative mechanisms; (5) establishing mechanisms for the development and environmentally sound application of biotechnology.

If biotechnology is to be used safely and effectively, its regulation needs to be a component of the national regulatory framework in the relevant sector. It is this that is necessary to ensure the safe and timely introduction of new products, not the biosafety component alone. For example, in the agricultural sector, the regulatory system needs to cover plant and animal quarantine, the approval of new plant varieties, the regulation of pesticides, the production of vaccines, and the use of biocontrol agents, as well as biosafety.

One option under discussion is to consider the need for, and the feasibility of, an international code of conduct (or legal instrument) on biosafety. To establish international legal means of control for biosafety would be a departure from the experience acquired during the development of biotechnology in OECD countries. All OECD countries regulate biotechnology on the basis of guidelines or national legislation. Further, different approaches are being taken by various OECD members, based on the OECD Council's guidance documents on "good development practices," which provide the basis for the development of national approaches.

The imposition of an international legal framework on regulating biotechnology may be seen by individual countries as a "top-down" approach — rather than enabling each to determine its own strategies in light of the available information, the accumulating experience in modern biotechnology, and national priorities for the use of biotechnology in medicine, agriculture, and the environment. The strategies chosen are likely to differ, depending on the size of the country, the environmental and development challenges it faces, the strength of its science and technology sector, and whether it is primarily a developer or an importer of technology.

A useful outcome from UNCED would be for all countries to examine UNIDO's voluntary *International Code of Conduct on the Release of Organisms into the Environment* and to establish an "enabling mechanism" to provide advice, on request, to individual countries seeking to establish a national regulatory framework for the use of biotechnology.

Appendix A
Additional Sources of Information

Africa

Côte d'Ivoire

Dr. Gaston Grenier Director General	Institut International de Recherche Scientifique pour le Developpement en Afrique (IIRSDA) B. P. V51 Abidjan, Côte d'Ivoire	Telephone: Fax:	225-454170 225-456828

Kenya

Dr. John Doyle Deputy Director General	International Laboratory for Research in Animal Diseases (ILRAD) Nairobi, Kenya	Telephone: Fax:	254-2-63211 254-2-631499
Dr. Calestous Juma Director	African Centre for Technology Studies P. O. Box 45917 Nairobi, Kenya	Telephone: Fax:	254-2-744047 254-2-743995

Zimbabwe

Prof. C. Chetsanga Pro-Vice-Chancellor	University of Zimbabwe P. O. Box MP167 Mount Pleasant Harare, Zimbabwe	Telephone: Fax:	263-4-303211 263-4-732828

Asia

ASEAN

Prof. Yongyuth Yuthavong Chair	ASEAN Subcommittee on Biotechnology National Center for Genetic Engineering and Biotechnology National Science and Technology Development Agency Rama VI Road Bangkok 10400, Thailand	Telephone: Fax:	66-2-245-2498 66-2-246-4850

India

Dr. S. Ramachandran Secretary **Dr. Manju Sharma** Senior Advisor **Dr. H. K. Srivastava** Project Coordinator	Department of Biotechnology Ministry of Science and Technology Block 2, 7th Floor, CGO Complex Lodgi Road New Delhi 110003, India	Telephone: Fax:	99-11-360598 91-11-362884

Indonesia

Dr. Ibrahim Manwan	Central Research Institute for Food Crops (CRIFC) Jalan Merdeka 147 Bogor 16111, Indonesia	Telephone: 62-251-324089 Fax: 62-251-325251
Dr. Setijati Sastrapradja Botanist	R&D Centre for Biotechnology Indonesian Institute of Sciences P. O. Box 323 Bogor Indonesia	Telephone: 62-251-321038 Fax: 62-251-321039

Australia

Dr. Nancy F. Millis Chairperson	Australian Genetic Manipulation Advisory Committee Department of Microbiology University of Melbourne Parkville, Victoria 3052 Australia	Telephone: 61-62-3344-5049 Fax: 61-62-3344-5104

Inter-American Institute for Cooperation in Agriculture (IICA), Costa Rica

Dr. Eduardo Trigo Director **Dr. Walter Jaffe** Specialist	Technology Generation & Transfer Program Inter-American Institute for Cooperation on Agriculture Box 55, 2200 Coronada San Jose, Costa Rica	Telephone: 506-290-222 Fax: 506-294-741

International Service for National Agricultural Research (ISNAR), The Hague

Dr. Barry Nestel Director	Research Policies and System Strategies International Service for National Agricultural Research P.O. Box 93375 2509 AJ The Hague, The Netherlands	Telephone: 31-70-349-6149 Fax: 31-70-381-9677

Organization for Economic Cooperation and Development (OECD), Paris

Dr. Peter Kearns **Dr. Victor Morgenroth** **Dr. Bruna Teso**	Organization for Economic Cooperation and Development 2, Rue André Pascal 75775 Paris Cedex 16, France	Telephone: 33-1-45-24-16-77 Fax: 33-1-45-24-16-75

Rockefeller Foundation

Dr. Gary Toenniessen	The Rockefeller Foundation 1133 Avenue of the Americas New York, NY 10036, USA	Telephone: 1-212-869-8500 Fax: 1-212-764-3468

Stanford University

Prof. John Barton	Stanford Law School Stanford University Stanford, CA 94305-8610, USA	Telephone: Fax:	1-415-723-2691 1-415-723-0253

United Nations Industrial Development Organization (UNIDO), Vienna

Dr. George Tzotzos Science Coordinator	International Centre for Genetic Engineering and Biotechnology (ICGEB) Vienna International Centre P.O. Box 300 Wadramer Strasse 5 A-1400 Vienna, Austria	Telephone: Fax:	43-1-211310 43-1-232156

United States Agency for International Development (USAID), Washington, DC

Dr. Joel Cohen Biotechnology and Genetic Resource Specialist	Room 412, SA-18, Office of Agriculture Bureau for Research & Development US Agency for International Development Washington, DC 20523-1809, USA	Telephone: Fax:	1-703-875-4219 1-703-875-5490
Dr. John Dodds Managing Director	USAID Project Agricultural Biotechnology for Sustainable Productivity Michigan State University 416 Plant and Soil Science Building East Lansing, MI 48823, USA	Telephone: Fax:	1-517-336-1641 1-517-336-1982

United States Department of Agriculture (USDA), Washington, DC

Mr. Terry Medley, Esq. Director **Dr. John Payne** Associate Director **Dr. L. Val Giddings** Senior Geneticist **Dr. Sally McCammon** Senior Plant Pathologist	Biotechnology, Biologics, & Environmental Protection Animal & Plant Health Inspection Service U.S. Department of Agriculture 6505 Belcrest Rd. Hyattsville, MD 20782, USA	Telephone: Fax:	1-301-436-7601 1-301-436-8724

World Bank, Washington, DC

Dr. Gabrielle Persley Biotechnology Manager	Agriculture and Rural Development Department The World Bank 1818 H Street, NW Washington, DC 20043, USA	Telephone: Fax:	1-202-473-0353 1-202-334-0568

Appendix B
Annotated Bibliography

Hall, P. 1991. Applying Biotechnology in Developing Countries: Biosafety and Risk Assessment Issues in International Biotechnology Transfer. (mimeo) 166p.

This report was prepared for the Resources Development Foundation and the Stockholm Environment Institute. It reviews the present status of biosafety in relation to the application of biotechnology in developing countries.

IICA. 1988. Guidelines for the Use and Safety of Genetic Engineering Techniques or Recombinant DNA Technology. Washington, DC: Inter-American Institute for Cooperation on Agriculture. 134pp.

This is an inter-American effort to provide safety assurance and regulatory guidance on a range of biotechnology issues including research done in laboratories or contained facilities, as well as research involving products intended for release. It gives some specific attention to the needs and constraints faced by Latin American countries, including advice on how national and institutional review bodies might be established, where they do not now exist. This publication resulted from a joint effort by IICA, the Pan American Health Organization/World Health Organization (PAHO/WHO), the Organization of American States (OAS), and the International Office of Epizootics (IOE).

IICA. 1991. Guidelines for the Release into the Environment of Genetically Modified Organisms. Washington, DC: Inter-American Institute for Cooperation on Agriculture. 137pp.

This booklet recommends guidelines for the release into the environment of genetically modified organisms, as determined by an Inter-American study group that met in Brasilia in June 1990. It represents a continuation of the IICA study described above.

Levin, M. A. and H. S. Strauss, eds. 1991. Risk Assessment in Genetic Engineering. New York: McGraw-Hill.

This book contains chapters from 18 authors on most aspects of risk assessment and regulation of environmental biotechnology, including one by Cohn and Chambers on biotechnology and biosafety in the developing world.

Millis, N. F. 1990. Regulating Release of Organisms. In *Agricultural Biotechnology: Opportunities for International Development*, edited by G. J. Persley. Wallingford, UK: CAB International.

This succinct chapter outlines the issues regarding regulation and safety assurance for biotechnology products, in particular, genetically modified organisms intended for uncontained environmental use. It makes specific policy suggestions linked with criteria for decision making. It provides advice and examples for establishing review bodies and the kinds of factors that need to be considered in their deliberations.

NAS. 1987. Introduction of Recombinant DNA-Engineered Organisms with the Environment: Key Issues. Washington,

DC: National Academy of Sciences, National Academy Press.

This booklet outlines the findings of a National Academy of Sciences study on the scientific basis of field releases of genetically engineered organisms.

NRC. 1989. Field Testing Genetically Modified Organisms: Framework for Decisions. Washington, DC: National Research Council, National Academy Press.

Produced by the US National Academy of Sciences, this study examines the relationship between products of the techniques of modern biotechnology and more traditional methods and points out factors helpful to regulatory decision makers in assuring safety.

OECD. 1986. Recombinant DNA Safety Considerations. Paris: Organization for Economic Cooperation and Development. 67pp.

This document outlines an approach to safety assurance/risk assessment and management that has been formally adopted by OECD member countries. It represents the first major step towards international harmonization of approaches to safety assurance for biotechnology products and outlines a rational approach based on sound science and effective regulatory strategies.

OECD. 1990. Good Developmental Principles: Guidance for the Design of Small-Scale Field Research with Genetically Modified Plants and Micro-Organisms. DSTI/STP/BS(90)1. Paris: Organization for Economic Cooperation and Development. 30pp.

This study builds on the 1986 OECD report to provide sound policy guidance for safety assurance in small-scale field tests of genetically modified organisms.

OECD. 1991. A Discussion Paper on Performance Trials for the Development of Plant Cultivars. Paris: Organization for Economic Cooperation and Development. 56pp.

This discussion paper builds on the earlier OECD papers on small-scale field tests to provide guidance for the next major step — large-scale or performance-trial plantings of genetically modified organisms.

OECD. 1992. Safety Considerations for Biotechnology — 1992. Paris: Organization for Economic Cooperation and Development.

This document is a follow-up to the 1986 OECD publication of the first international safety guidelines for biotechnology. The document elaborates on safety criteria for good industrial large-scale practice (GILSP) for the handling of low-risk recombinant-DNA microorganisms and cell cultures in industrial production. It also defines good development principles (GDP) for the design of safe, small-scale field research with genetically modified plants and microorganisms. It is a major contribution in developing safe and effective biosafety procedures in the laboratory and in the field.

OTA. 1988. Field-Testing Engineered Organisms: Genetic and Ecological Issues. Lancaster, PA: Technomic Publishing Co., Inc. 150pp. (Originally published as New Developments in Biotechnology, 3, OTA-BA-350. Washington, DC: US Government Printing Office.)

This book provides a comprehensive view of the genetic, ecological, and public-policy issues relevant to the products of the new biotechnologies likely to be used in the field.

Persley, G. J. 1990a. Beyond Mendel's Garden: Biotechnology in the Service of World Agriculture. Wallingford, UK: CAB International. 155pp.

This book provides a succinct introduction to the potential of biotechnology for agriculture. Especially helpful to the nonexpert, it examines the range of critical factors that will have an impact on how quickly, broadly, and safely this potential is realized. It summarizes the findings of a major study on the likely applications of biotechnology in agriculture in developing countries cosponsored by the World Bank, ISNAR, and the Australian Government.

Persley, G. J. 1990b. Agricultural Biotechnology: Opportunities for International Development. Wallingford, UK: CAB International. 495pp.

This edited collection of 33 papers by internationally recognized experts provides useful background information on a wide range of topics relevant to biotechnology applications and international development. It represents the commissioned papers from an agricultural biotechnology study cosponsored by the World Bank, ISNAR, and the Australian Government.

Tiedje, J. M., R. K. Colwell, Y. L. Grossman, R. E. Hadson, R. E. Linski, R. N. Mack and P. J. Regal. 1989. The Planned Introduction of Genetically Engineered Organisms: Ecological Considerations and Recommendations. *Ecology* 70: 298-315.

This report of the Ecological Society of America describes risk-assessment procedures suitable for dealing with genetically modified organisms and provides a framework for risk assessment.

UNIDO. 1991. Voluntary Code of Conduct for the Release of Organisms into the Environment. Vienna: United Nations Industrial Development Organization.

This document outlines a voluntary code of conduct prepared by the UNIDO Secretariat and an expert working group on behalf of the UNIDO/UNDP/WHO/FAO working group on biosafety.

USDA. 1992. List of Permits Issued. Washington, DC: United States Department of Agriculture, Animal and Plant Health Inspection Service: Biotechnology, Biologics and Environmental Protection Division (USDA/APHIS/BBEP).

USDA/APHIS/BBEP is the US Government regulatory authority charged with protecting US agriculture from potential risks. It issues permits for small-scale field testing of genetically engineered organisms. Each permit is issued only after a site-specific environmental assessment (EA) has been conducted and no significant environmental impact is deemed likely to result from the field test. All environmental assessments are publicly available. The permit list provides an up-to-date indication of the direction and extent of R&D activity, as well as an index to EAs that may be of further interest. Copies of the current list are available on request from USDA/APHIS/BBEP, 6005 Belcrest Road, Hyattsville, MD 20782, USA.

US Office of Science and Technology Policy. 1992. Exercise of Federal Oversight within Scope of Statutory Authority: Planned Introductions of Biotechnology Products into the Environment. *Federal Register* 57(39): 6753-6762.

This document presents the latest statement of US policy on the topic. It outlines regulatory procedures and guidelines for reducing government oversight for

biotechnology products for which sufficient experience has been gathered.

US President's Council on Competitiveness. 1991. Report on Biotechnology Policy. Washington, DC: US Government Printing Office. 26pp.

This document outlines the US Government's perspective on how best to provide the necessary safety assurance for biotechnology products.

Note: The publications listed here are available directly from their authors/institutions. Should interested readers experience any difficulty in obtaining them, they may contact Dr. G. J. Persley, who also retains most of them (Addre·· Agriculture and Rural Development Department, World Bank, 1818 H Street, NW, Washington, DC 20433, USA; Fax: 1-202-334-0568).

Appendix C
Glossary

Amino Acid
Any one of a group of 20 chemicals that are linked together in various combinations to form proteins. Each protein is made up of a specific sequence of these chemicals. This unique sequence is coded for by a **gene**.

Anticodon
A particular combination of three **bases** in **transfer RNA** that is complementary to a specific three-base codon in messenger RNA. Alignment of codons and anticodons is the basis for organizing amino acids into a specific sequence in a protein chain.

Bacterium
Any one of a group of one-celled microorganisms having round, rodlike, spiral, or filamentous bodies that are enclosed by a cell wall or membrane and lack fully differentiated nuclei.

Base
The units of a nucleic acid. In DNA, the four bases are adenine (A), guanine (G), cytosine (C), and thymine (T). In RNA, the base uracil (U) replaces thymine. Bases are sometimes called *nucleotides*.

Base-pairing rule
Two bases, one in each strand of a double-stranded DNA molecule, are attracted to one another on the basis of their chemical structure: G (guanine) always pairs with C (cytosine), and A (adenine) pairs with T (thymine) in DNA or with U (uracil) in RNA. Based on the sequence of bases in one strand of DNA, it is possible to predict the sequence in the opposite, complementary, strand.

Biosafety
The policies and procedures adopted to ensure the environmentally safe applications of biotechnology.

Biotechnology
Any technique that uses living organisms or substances from these organisms to make or modify a product, to improve plants or animals, or to develop microorganisms for specific uses.

Cell
The smallest component of life. A membrane-bound protoplasmic body capable of carrying on all essential life processes. A single cell unit is a complex collection of molecules with many different activities.

DNA sequencing
Determination of the order of bases in a DNA molecule.

Enzyme
A protein that accelerates a specific chemical reaction, without itself being destroyed.

Gene
The fundamental physical and functional unit of heredity, the portion of a DNA molecule that is made up of an ordered sequence of nucleotide base pairs that produce a specific product or have an assigned function.

Genetic code
The code that translates information contained in messenger RNA into amino acids. Different triplets of bases (called codons) code for each of 20 different amino acids.

Genetic engineering
Technologies (including recombinant-DNA technologies) used to isolate genes from an organism, manipulate them in the laboratory, and insert them into another organism.

Genotype
The genetic constitution of an organism as distinguished from its physical appearance (phenotype).

Germ plasm
The total genetic variability, represented by germ cells or seeds, available to a particular population of organisms.

Hybrid
An offspring of a cross between two genetically unlike individual plants or animals.

Hybridoma
A new cell resulting from the fusion of a myeloma cell (a type of tumor cell that divides continuously in culture) with a lymphocyte (an antibody-producing cell). Cultures of such cells are capable of continuous growth and specific (i.e., monoclonal) antibody production.

Intellectual property
That area of the law involving patents, copyrights, trademarks, trade secrets, and plant variety protection.

Ligase
An enzyme that joins the ends of DNA molecules together. These enzymes are essential tools in genetic engineering.

Monoclonal antibodies
Identical antibodies that recognize a single, specific antigen and are produced by a clone of specialized cells.

Restriction enzyme
Bacterial enzymes that recognize specific short sequences of DNA and cut the DNA where these sites occur.

RFLP
Restriction fragment length polymorphisms — fragments of differing lengths of DNA that distinguish individuals, produced by cutting with restriction enzymes. They result from variations in the DNA sequence and can be detected with radioactive probes and used as markers in breeding.

RNA (ribonucleic acid)
Nucleic acid complementary to DNA — the three kinds of RNA important in the genetic processes in cells are messenger RNA (mRNA), ribosomal RNA (rRNA) and transfer RNA (tRNA).

Species
Reproductive communities and populations that are distinguished by their collective manifestation of ranges of variations with respect to many different characteristics and qualities.

Tissue culture
The propagation of tissue removed from organisms in a laboratory environment that has strict sterility, temperature, and nutrient requirements.

Transcription
The process of converting information in DNA into information contained in messenger RNA.

Transfer RNA (tRNA)
RNA that is used to position amino acids in the correct order during protein construction.

Transformation
Introduction and assimilation of DNA from one organism to another via uptake of naked DNA.

Transgenic animals or plants
Animals or plants whose hereditary DNA has been augmented by the addition of DNA from a source other than parental germ

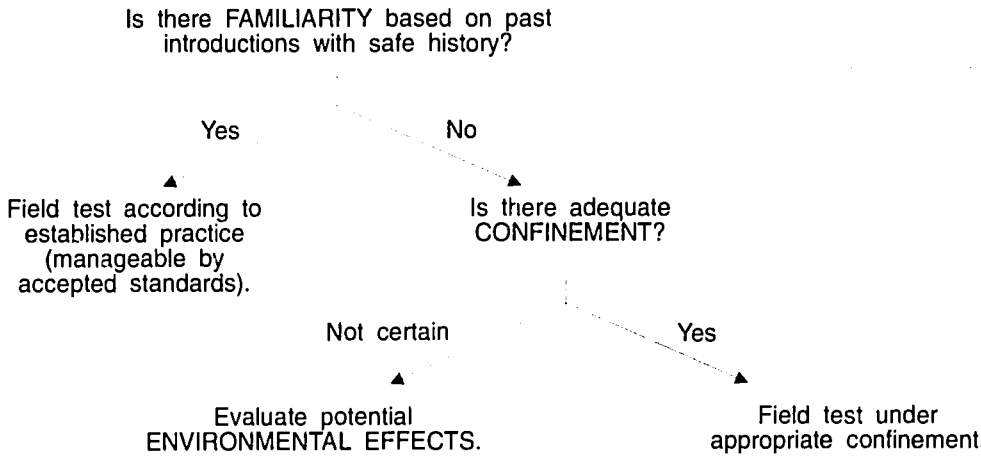
plasm, in a laboratory using recombinant-DNA techniques.

Translation
The process of converting the information in messenger RNA into protein.

Vector
A carrier or transmission agent. In the context of recombinant-DNA technology, a vector is the DNA molecule used to introduce foreign DNA into host cells. Recombinant-DNA vectors include plasmids, bacteriophages, and other forms of DNA.

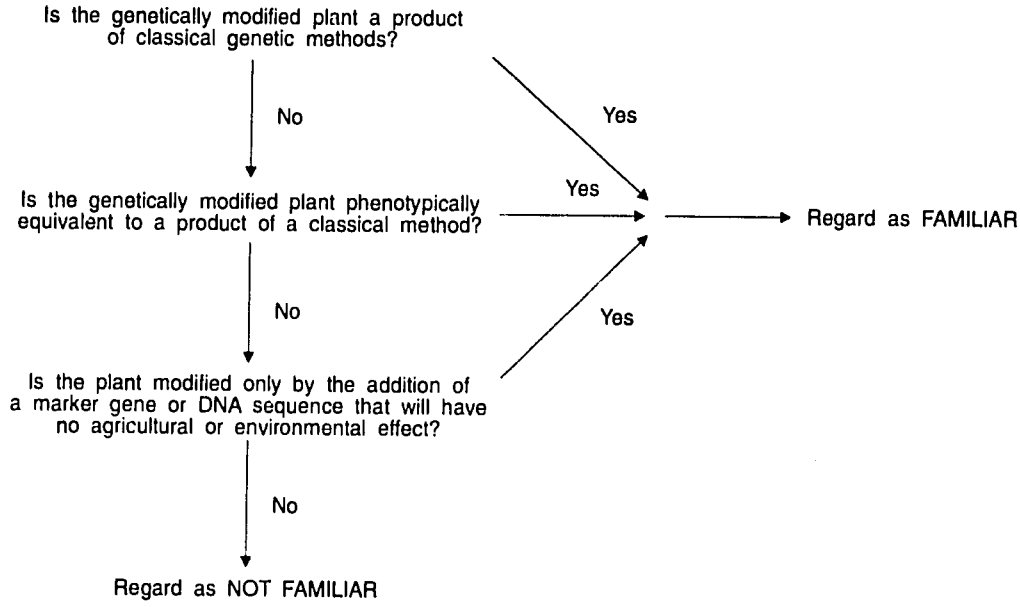
Source: Persley (1990b).

Appendix D
Framework for Risk Assessment



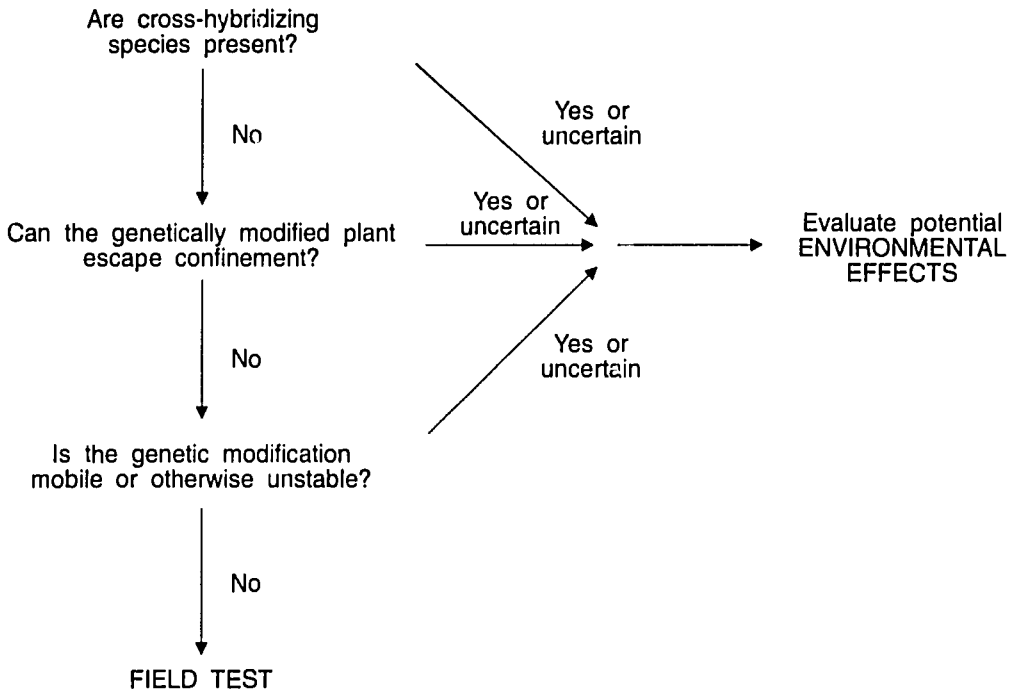
Source: Modified from NRC (1989).

Appendix Figure 1. Framework to assess field testing of genetically modified plants



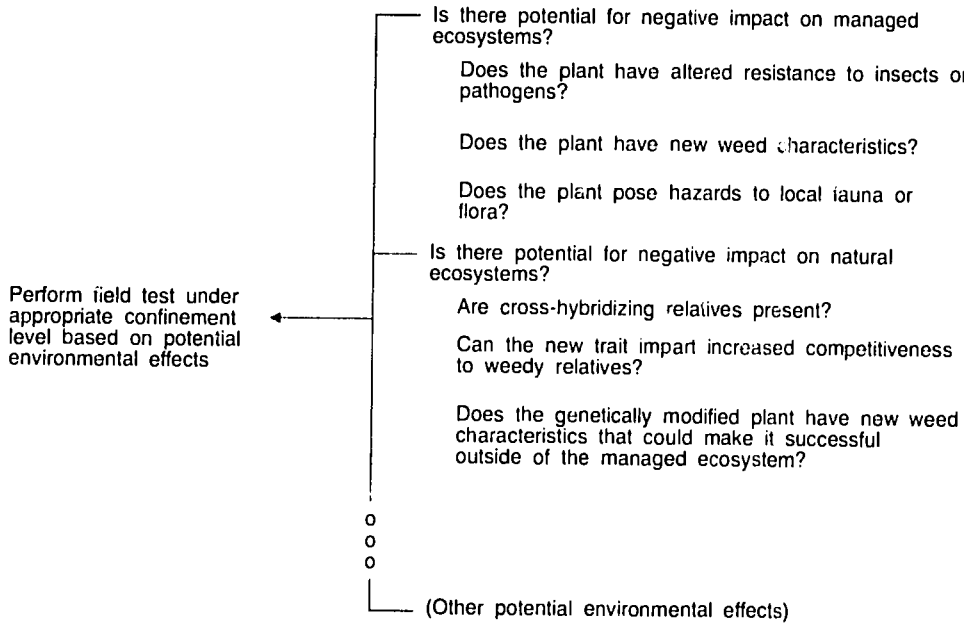
Source: Adapted from NRC (1989)

Appendix Figure 2. Familiarity tests for genetically modified plants



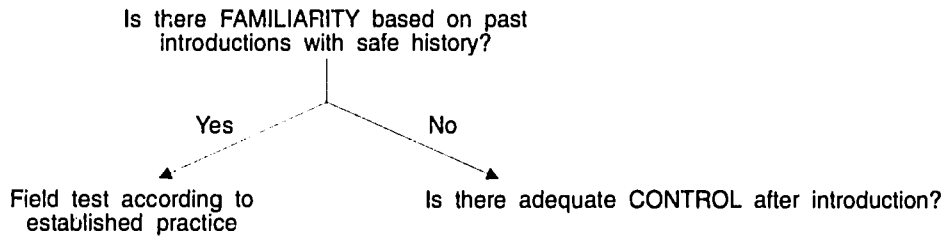
Source: Modified from NRC (1989).

Appendix Figure 3. Confinement tests for genetically modified plants



Source: Modified from NRC (1989).

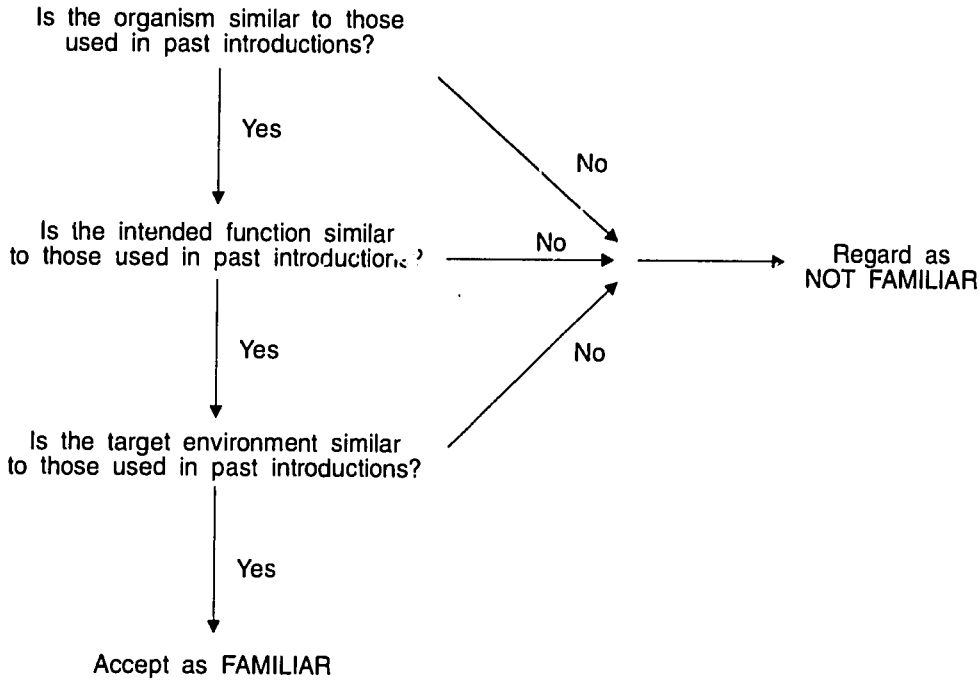
Appendix Figure 4. ***Potential environmental effects:*** **appropriate questions for specific applications to be added by users of the framework for release of genetically modified plants**



Have significant adverse environmental EFFECTS been reasonably excluded?	Yes	No
Yes	Low uncertainty	Moderate uncertainty
No	Moderate uncertainty	High uncertainty

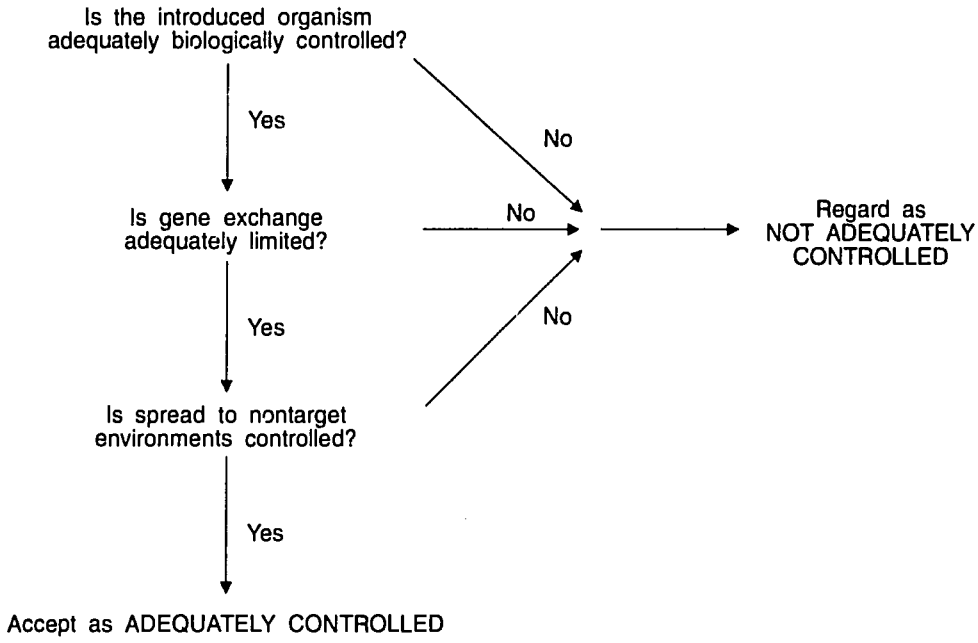
Source: Modified from NRC (1989).

Appendix Figure 5. Framework to assess field testing of genetically modified microorganisms



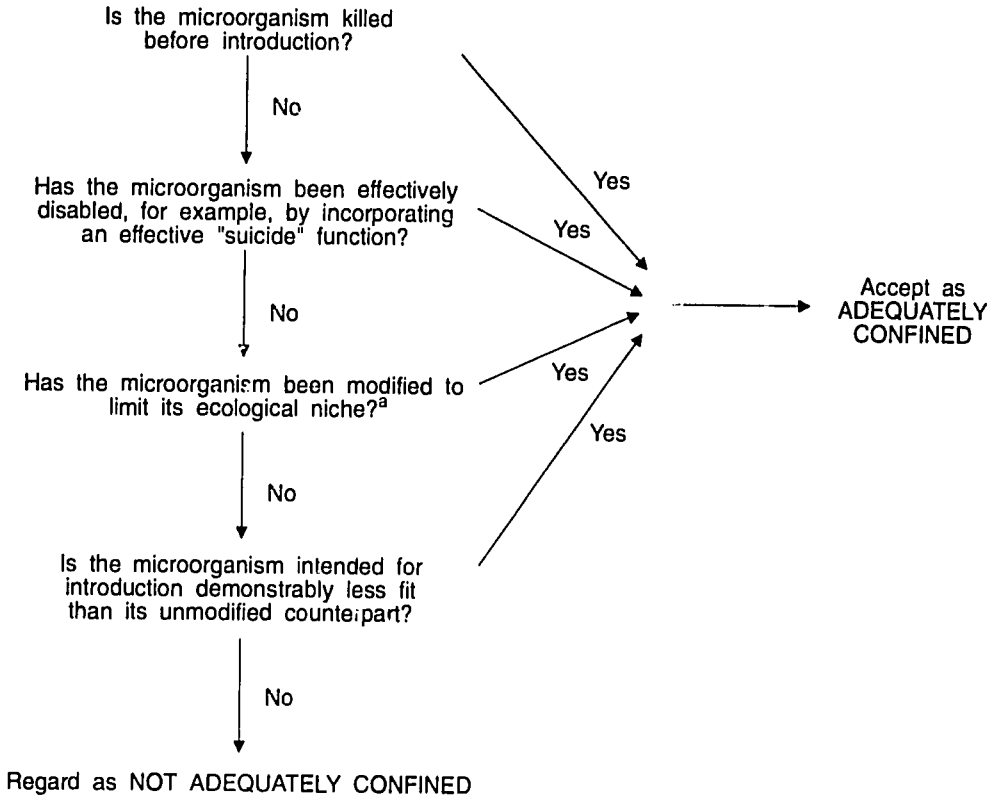
Source: Adapted from NRC (1989).

Appendix Figure 6. Familiarity tests for genetically modified microorganisms



Source: Modified from NRC (1989).

Appendix Figure 7. ***Control:*** **Appropriate questions for specific applications to be added by users of the framework for the release of genetically modified microorganisms**



Source: Modified from NRC (1989).
Note: With respect to substrate utilization, host range, physiological tolerance, resistance, or competitiveness.

Appendix Figure 8. ***Biological confinement:*** **Appropriate questions for specific applications to be added by users of the framework for the release of genetically modified microorganisms**

What is the intended function of the introduced organism?

- **Microbial enhancement of plant nutrition**

  For example, is the intended function, if carried out in excess, potentially detrimental to the target environment?

- **Microbial biodegradation of toxic pollutants**

  For example, is it possible that toxic compounds could be produced as by-products of the microorganism's biodegradative activities?

- **Microbial biocontrol of pest populations**

  For example, is the biocontrol agent specific to the target pest population or might it also be toxic or pathogenic to other organisms (including plants, invertebrates, or vertebrates) in the environment?

o
o
o

- (Other potential environmental effects)

Source: Modified from NRC (1989).

Appendix Figure 9. ***Potential environmental effects:*** **Appropriate questions for specific applications to be added by users of the framework for the release of genetically modified microorganisms**