MODULE C

# Biosafety Resource Book

## RISK ANALYSIS

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MODULE C

# LIST OF ABBREVIATIONS

**ABS** Access and benefit-sharing
**AIA** Advanced Informed Agreement
**ASEAN** Association of Southeast Asian Nations
**BCH** Biosafety Clearing-House
**CBD** Convention on Biological Diversity
**Codex** Codex Alimentarius
**COP-MOP** Conference of the Parties serving as the meeting of the Parties to the Protocol
**CPB** Cartagena Protocol on Biosafety
**CPM** Commission on Phytosanitary Measures
**DNA** Deoxyribonucleic acid
**EC** European Commission
**EIA** Environmental Impact Assessment
**EU** European Union
**FAO** Food and Agriculture Organization of the United Nations
**FFP** Food, or feed or for processing
**GATT** General Agreement on Tariffs and Trade
**GDP** Good Development Principles
**GMO** Genetically modified organism
**IP** Identity preservation
**IPPC** International Plant Protection Convention
**ISPM** International Standard for Phytosanitary Measures
**ITPGRFA** International Treaty on Plant Genetic Resources for Food and Agriculture
**IUCN** International Union for Conservation of Nature
**LMO** Living modified organism
**NGO** Non-governmental organization
**OECD** Organisation for Economic Co-operation and Development
**OIE** Office International des Epizooties
**PGRFA** Plant Genetic Resources for Food and Agriculture
**PRA** Pest Risk Analysis
**SPM** Sanitary and Phytosanitary Measures
**SPS** Sanitary and Phytosanitary Agreement
**TBT** Technical Barriers to Trade
**TRIPS** Agreement on Trade-related Aspects of Intellectual Property Rights
**UN** United Nations
**UNECE** United Nations Economic Commission for Europe
**UNEP** United Nations Environment Programme
**UNIDO** United Nations Industrial Development Organization
**UPOV** International Union for the Protection of New Varieties of Plants
**USDA** United States Department of Agriculture
**WHO** World Health Organization
**WTO** World Trade Organization

CHAPTER 1

# BIOLOGICAL RISKS: BASIC CONCEPTS AND CLASSIFICATION

## 1.1 BIOLOGICAL RISKS

The objective of a **biosafety** system is to prevent, manage, minimize or eliminate hazards to human health and security and to protect the environment from biological agents and organisms used in research and trade. The following terminologies associated with biological risks are defined or described:

**Biological agents** - living organisms, or materials derived from them, which can potentially cause diseases in, or harm to, humans or the environment.

**Hazard** – a hazard can be described in general terms as "*a situation in which particular circumstances represent a danger*", that is, the potential for an adverse occurrence. One example is a threat to the quality of life of an individual or a group.

**BIOSAFETY**
To prevent, manage, minimize or eliminate hazards to human health and security and to protect the environment from biological agents and organisms used in research and trade.

**BIOLOGICAL AGENTS**
Living organisms, or materials derived from them, which can potentially cause diseases in, or harm to, humans or the environment.

**HAZARD**
A situation in which particular circumstances represent a danger.

**BIOLOGICAL HAZARDS**
Infectious agents or hazardous biological materials that present a risk, or potential risk, to the health of humans, animals or other organisms.

**Biological hazards, or biohazards** - *are those infectious agents or hazardous biological materials that present a risk, or potential risk, to the health of humans, animals or other organisms*. The risk can be manifested directly through infection, or indirectly through damage to the environment. Unlike chemical hazards, infectious agents have the ability to reproduce and to give rise to large numbers of infectious organisms/particles, starting from a small amount of initially released material. Biological hazards are numerous and diverse.

An overview of biological hazards is presented in Table 1.1:

Table 1.1 | **Definitions of hazard as applicable to different biosecurity sectors**

| | |
|---|---|
| **Food safety** | A biological, chemical or physical agent in, or condition of, food with the potential to cause an adverse health effect |
| **Zoonoses** | A biological agent that can be transmitted naturally between wild or domestic animals and humans |
| **Animal health** | Any pathogenic agent that could produce adverse consequences on animal health |
| **Plant health** | Any species, strain or biotype of plant, animal or pathogenic agent injurious to plants or plant products |
| **Plant health quarantine** | A pest of potential economic importance to the area endangered thereby and not yet present there, or present but not widely distributed and being officially controlled |
| **"Biosafety" in relation to plants and animals** | A living modified organism (LMO) that possesses a novel combination of genetic material obtained through the use of modern biotechnology that is likely to have adverse effects on the conservation and sustainable use of biological diversity, taking into account also risks to human health |
| **"Biosafety" in relation to food** | A recombinant DNA organism directly affecting or remaining in a food product that could have an adverse effect on human health |
| **Invasive alien species** | An invasive alien species outside its natural past or present distribution whose introduction and/or spread threatens biodiversity |

*Adapted from*: FAO, 2007.

**BIOLOGICAL RISK**
The risk associated with a biological agent or organism is the probability of the occurrence of a particular adverse event at a specific time and the magnitude of the consequent damage caused.

**Biological risks** - The risk associated with a hazard can be considered as the potential for a hazard having adverse consequences on human existence and health, property and the environment under specific conditions. The risk is therefore a combination of two factors: the probability and the consequence of an adverse

occurrence. Thus the risk associated with a biological agent or organism is the probability of the occurrence of a particular adverse event at a specific time and the magnitude of the consequent damage caused, depending on various factors such as exposure to the hazard, the frequency of exposure and the severity of any consequent damage done. Many aspects of risk analysis are generic and can be applied to all classes of risk. Risk is a measure of the probability and severity of adverse effects.

It can be expressed as follows: **RISK = likelihood x consequence**

**RISK**
Likelihood of occurrence x consequence of an incident.

Biological risks can be classified into two broad categories: naturally occurring or human-caused:

- *Naturally occurring biological risks* include:
  (1) the emergence of antibiotic resistant bacterial infections (tuberculosis, pneumonia, flu epidemic);
  (2) naturally emerging pathogens attributed to deforestation (monkeypox, Ebola, Lassa fever);
  (3) spreading of a zoonosis, i.e. infected animal populations conveying the disease to humans via direct contact, vectors or water/foodstuffs;
  (4) toxins arising from certain molds and fungi (deoxynivalenol, aflatoxins, ochratoxin );
  (5) parasitic infection outbreaks in humans;
  (6) invasive alien species (plants, animals and micro-organisms).

- *Human-caused or related biological risks,* which can be further classified into:
  (1) deliberately induced risks such as the use of harmful biological agents through warfare or terrorism; and
  (2) biotechnological risks such as products of traditional cross-breeding and selection, mutation and modern biotechnology.

According to the hazard and the associated risk, hazard-based and risk-based measures can be taken:

| WORKING DEFINITIONS FOR HAZARD-BASED AND RISK-BASED CONTROL MEASURES |
| --- |
| **Hazard based** – A control measure that is based on quantified and verifiable information on the level of hazard control that is likely to be achieved but lacking quantitative knowledge of the level of protection that is likely to result. |
| **Risk-based** – A control measure that is based on quantitative and verifiable information on the level of protection that is likely to be achieved. |

*Adapted from*: FAO, 2007.

## 1.2 CLASSIFICATION OF BIOLOGICAL AGENTS

The need to classify biological agents according to their risk arises from the high incidence of diseases contracted by people and because of the possible danger of spreading pathogenic agents in the environment. Furthermore, the growing field of biotechnology and the advances in genetic engineering require detailed analyses of the risks associated with genetically modified organisms. Those in contact with infectious biological agents, genetically modified material or any other potentially harmful biological agent must be made aware of the potential dangers that are associated with and the characteristics of the agents. Education in safe handling of such agents, using appropriate techniques, needs to be made available.

The personnel of research institutions, biomedical firms and veterinary quarantine services are among those that teach, research, produce and control biological materials or foods and feeds. Such materials can potentially represent sources of direct infection, by containing pathogenic micro-organisms. Moreover, the environment could become contaminated if an accidental escape of biological agents were to occur. Therefore, detailed knowledge about the classification of biological agents and material is required to assure appropriate handling and minimize potential risks.

## 1.3 BIOLOGICAL AGENTS AND RISK GROUPS

One way to **classify biological risks** is based on the risk posed by biological agents to human health and the environment upon accidental or intentional release. Biological agents are typically used in research or biomedical laboratories, and include the full range of micro-organisms: bacteria, viruses, fungi, protozoa and multicellular parasites. Laboratory acquired infections (LAI) have been documented since the beginning of the twentieth century. However, the advent of modern biotechnology raised awareness about the hazards of infectious micro-organisms and the risks they pose to laboratory workers who handle them, and to the community if they escape from the laboratory.

**BIOLOGICAL RISK CLASSIFICATION**
Based on the risk posed by biological agents to human health and the environment upon accidental or intentional release.

There are three ways that bring workers into contact with materials that may pose a biological risk. These are:

- ***Exposure*** *as a result of working with biological agents* – areas of work include microbiology laboratories, greenhouses and animal houses. Activities include isolation, identification and culture of micro-organisms or cells, including materials used for genetic modification and intentional contact with animals, plants and materials that originate from animals and plants as part of the experimental work.
- *Exposure which does not result from the work itself but is incidental to it, mainly because biological agents are present as contaminants* - areas and activities include farming, refuse collection, sewage treatment, handling human body fluids and excreta, and handling materials that may be contaminated by these materials, such as hypodermic needles or sewage treatment plants.
- *Exposure which is not a result of work* – unintentional contact with animals or animal and plant materials or people, in the workplace or elsewhere.

**EXPOSURE**
The contact to biological agents that may represent a danger to human health or the environment.

The World Health Organization (WHO, 2004) has recommended an agent **risk group** classification for laboratories, aimed at defining the appropriate containment levels

**RISK GROUPS**
Four risk groups for biological agents were defined, based on factors such as pathogenicity, mode of transmission, availability of preventive measures and treatment.

required to protect people working with biological agents and ensuring they do not get infected, based on risk criteria/factors described below:

- *Pathogenicity of the agent or its product* - inherent risks of a pathogen are based on factors such as the severity of the disease it causes, its virulence and infectivity. Diseases caused by products of a biological agent include toxicity, allergenicity, and modulation of physiological activity.
- *Mode of transmission and host range of the agent* – these are influenced by existing levels of immunity, density and movement of the host population, presence of appropriate vectors and standards of environmental hygiene.
- *Availability of effective preventive measures* - these may include: prophylaxis by vaccination or antisera; sanitary measures, e.g. food and water hygiene; the control of animal pathogen reservoirs or arthropod vectors; the movement of people or animals; and controlling the importation of infected animals or animal products.
- *Availability of effective treatment* - includes passive immunization and post-exposure vaccination, antibiotics, and chemotherapeutic agents, taking into consideration the possibility of emergence of resistant strains.

Other considerations that may be taken into account in classifying biological agents include:

- *Origin/source* – indigenous (native, local) or exotic (foreign, alien) origin; exotic agents pose higher risks to human health because they may cause more severe infections with no available treatment.
- *Ability of the organism to survive* – dormancy or resting period during unfavourable conditions.
- *Number/concentration of pathogens* – the higher the number and concentration of a pathogen, the greater the likelihood of infection.
- *Nature and route of transmission* – inhalation (dust, aerosol), ingestion (food, drink, saliva), direct contact (cuts, bites, injection).

The *National Institute of Health, USA (*NIH, 2002*)* established a **classification of genetically modified agents** into a particular risk group using the same criteria indicated above. Many countries have adopted the WHO and NIH risk group classifications and criteria.

**GMO CLASSIFICATION**
Classicication of GMOs into four risk groups, according to the potential danger they represent.

The four resulting WHO and NIH risk groups are presented below in Table 1.2:

Table 1.2 | **Risk group classification of biological agents**

| RISK GROUP Classification | NIH Guidelines For Research Involving Recombinant DNA Molecules, 2002 | World Health Organization Laboratory Biosafety Manual 3rd Edition 2004 |
|---|---|---|
| **Risk Group I** | Agents that are not associated with disease in healthy adult humans | A micro-organism that is unlikely to cause human disease or animal disease. (No or low individual and community risk.) |
| **Risk Group II** | Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often available | A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock, or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread is limited. (Moderate individual risk; low community risk.) |
| **Risk Group III** | Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions may be available. | A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available. (High individual risk; low community risk.) |
| **Risk Group IV** | Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available. | A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available. (High individual and community risk.) |

*Adapted from*: BMBL, 2007.

Using the above criteria of classification, hazard groups can be summarized in the following scheme (Table 1.3):

Table 1.3 | **Hazard group classification**

| Hazard Group | Pathogenicity for humans | Hazard to workers | Spread to the community | Effective prophylaxis or treatment |
|---|---|---|---|---|
| 1 | Unlikely to cause human disease | Low | Unlikely | Available |
| 2 | Can cause human disease | Intermediate | Unlikely | Usually available |
| 3 | Can cause severe human disease | Likely/ possibly serious | May spread | Usually available |
| 4 | Causes severe human disease | Serious | Likely | Unavailable |

The four-risk group classification of biological agents is widely recognized but disagreements exist in allocating agents to a particular risk group. WHO recommends each country draw up its own classification by risk group of the agents encountered in that country based on the above-mentioned criteria and considerations.

### 1.3.1 Classification of biological agents that affect animals

**BIOLOGICAL AGENTS AFFECTING ANIMALS/ PLANTS**
As for human pathogens and potentially dangerous biological agents, risk groups for classification of animal/plant pathogens have been defined.

The classification of the WHO is used in the initial stages of establishing laboratory biosafety procedures, but is not strictly applicable to animals. Instead, a working group within the International Veterinary Biosafety Working Group recommended that biological agents that affect animals be classified into four risk groups:

» Low risk animal pathogens: Agents that cause diseases of minor importance for animal health and for which transmission is poor.

- Moderate risk animal pathogens: Agents that cause diseases with a moderate risk of transmission with a certain level of morbidity, but seldom cause mortality.
- High risk animal pathogens: Agents that cause serious, easily transmissible diseases with a high level of morbidity and occasional mortality.
- Very high risk animal pathogens: There is a dual definition for this group. It includes pathogenic agents that cause serious diseases and which can be highly transmissible within the animal population. It also includes micro-organisms that cause serious diseases, are highly transmissible and are associated with high morbidity and mortality.

### 1.3.2 Classification of biological agents that affect plants

In the case of plants, the classification enables the definition of the risks for the environment resulting from handling of biological agents, facilitating therefore the development of criteria for biosafety procedures in plant facilities. Because some of these agents can affect human health they are included in the classification.

The European Federation of Biotechnology (EFB) developed the first system of classification in 1985, which was then revised in 1992 by the working group on biosafety of the same federation, and they proposed a new system for classification of micro-organisms causing plant diseases (Kuenzi *et al.*, 1987).

The factors affecting development of a disease include:

- inoculum density;
- resistance of the pathogen to environmental conditions (humidity, temperature, cultural practices and chemical application);
- means of dissemination: water, air, soil or vectors;

- presence of susceptible hosts;
- spatial relationship between susceptible hosts and pathogens;
- virulence of the pathogen.

The classification proposed by the working group was:

- Class 1. Micro-organisms that can cause diseases in plants of minor importance. They generally include indigenous species and do not require special biosafety measures to be worked with, except good laboratory practices (GLP).
- Class 2. Micro-organisms that cause important disease outbreaks in crops, ornamental plants and forests. Work with such pathogens is subject to national regulations.
- Class 3. Micro-organisms included on quarantine lists. Importation and handling of these is generally prohibited. Work with them generally requires authorization from national bodies.

For genetically modified organisms (GMOs), the four-risk group classification is employed depending on the risk associated with the selected donor, the recipient, the host-vector relationship and the resultant GMO.

CHAPTER 2

# THE RISK ANALYSIS PROCESS: BASIC CONCEPTS

**Risk analysis** can be broadly defined as an integrated process consisting of three major components: risk assessment, risk management and risk communication. The individual components are distinct, but are linked to achieve a well-functioning risk analysis process that forms the basis for decision-making on any operation or dealing of GMOs (Australian Government, 2005).

**RISK ANALYSIS**
An integrated process to analyse risk and form the basis for further decision-making.

In the case of biosafety, risk analysis involves a scientific process to estimate the risks to human life and health, as well as the impact on the environment, associated with the use of a particular GMO or its products. The prevention, reduction or elimination of these risks requires methods of risk management that are normally implemented as actions conforming to particular regulations. Risk assessment and risk management have to be implemented along with risk communication, which involves all interested parties and allows for an iterative process of risk analyses.

Risk assessment is important in the process of risk analysis given that if a particular risk is not identified, the steps taken to reduce it cannot be formulated in the risk management process. Risk assessment relies on a solid scientific base. Each case has to be dealt with individually and a separate evaluation has to be undertaken for each phase of obtaining, researching, testing, producing and releasing into

**RISK ASSESSMENT**
A rigorous science-driven process used to identify a hazard and obtain qualitative or quantitative estimates of the levels of risk posed by a hazard.

the environment of GMOs on a large or small scale. The complexity of the risk analysis process applied to a large variety of genes and gene combinations is very high, since this can result in a vast range of effects and interactions. In this sense, evaluation of possible impacts over the long term presents many difficulties. Moreover, the results of risk assessments from small-scale tests cannot be extrapolated to the large scale.

## 2.1 COMPONENTS OF RISK ANALYSIS

**Risk assessment** is the first and the *scientific component* of risk analysis. It is a rigorous science-driven process used to identify a hazard and obtain qualitative or quantitative estimates of the levels of risk posed by a hazard, including possible adverse effects on human health and the environment. It typically consists of four steps: (1) hazard analysis (identification and characterization), (2) likelihood estimation, (3) consequence evaluation; and (4) risk estimation. A more detailed discussion of risk assessment is presented in Chapter 3.

**RISK MANAGEMENT**
Is concerned with evaluating whether the risks identified by the risk assessment process are acceptable and manageable, then selecting and implementing the control measures as appropriate to ensure that risks are minimized or controlled.

**Risk management** is the second and *decision-making component* of the process of risk analysis. It is primarily supported by risk assessment but is also supported by other risk considerations. Risk management is concerned with evaluating whether the risks identified by the risk assessment process are acceptable and manageable, then selecting and implementing the control measures as appropriate to ensure that risks are minimized or controlled. A more detailed discussion on the methodology of risk management and other considerations is presented in Chapter 4.

**RISK COMMUNICATION**
The process of exchange of information and opinions concerning risk and risk-related factors among various stakeholders concerned with risk.

**Risk communication** is recognized as the third component that underpins the risk assessment and risk management processes. It is the process of exchange of information and opinions concerning risk and risk-related factors among various stakeholders concerned with risk (Codex Alimentarius Commission, 2003). It strengthens the overall process of risk analysis by helping to define the issues and

providing the link and the feedback mechanism that informs the two processes of risk assessment and risk management (FAO, 1999). The principles, structures and processes of risk communication are presented in Chapter 5.

The interplay between risk assessment, risk management and risk communication is depicted in Figure 2.1:

Figure 2.1 | **Generic components of risk analysis**


*Adapted from*: FAO, 2007.

Risk analysis applied in the broad sense separates the risk assessment from risk management. The reasons are: to maintain the scientific integrity of the risk assessment, to avoid confusion over the functions to be performed by risk assessors and risk managers, and to minimize any conflict of interest. In practice, however, this separation is rarely clear-cut and variation in its implementation exists among countries and across regulatory institutions.

## 2.2 PRINCIPLES OF RISK ANALYSIS: GENERAL ASPECTS

**PRINCIPLES OF RISK ANALYSIS**
General aspects of risk analysis have been defined that need to be maintained to assure reliability of the obtained results.

While regulatory frameworks for risk analysis vary among countries, the underlying general principles in assessing risks posed by GMOs to human health and the environment share many similarities. These include:

*Science-based* – Risk should be assessed using information obtained through application of science and scientific methods, i.e. rigorous and systematic, reproducible, with testable null hypothesis, qualitative and/or quantitative. Methods used should be appropriate and data generated of high quality to withstand scientific scrutiny and peer review.

*Open, transparent and documented* – All aspects of the process of risk analysis should be fully documented in a transparent manner. Documentation should be accessible to all interested parties, while respecting legitimate concerns to preserve confidentiality. This principle also refers to the selection of experts who will conduct the risk assessment. Experts responsible for risk assessment should be selected on the basis of their expertise, experience, and their independence with regard to the interests involved.

*Case by case* - Risk should be assessed on a case-by-case basis. This means that for each case, the risk assessment methodology and required information may vary in nature and level of detail, depending on the GMO concerned, its intended use (e.g. laboratory, field, market) and the likely potential of the receiving environment (e.g. presence of wild relatives, non-target species, endangered species, etc.).

*Comparative* - Risks should be compared with background risks, i.e. risks are considered in the context of the risks posed by the non-modified recipients or parental organisms, within the context of the intended use. This requires appropriate comparators and well-established baseline information.

*Systematic* - The risk analysis should follow a structured, step-by-step approach. The key steps are: establish the purpose, scope and boundaries of the risk assessment, assess the risk, and manage and communicate the risks.

*Iterative* - Risks should be evaluated and reviewed as appropriate in the light of newly generated scientific data. Conclusions and assumptions should be examined relative to new information.

*Inclusive* – The process of risk analysis should be all-encompassing. The three components of risk analysis should be applied within an overarching framework for management of food- or organism-related risks to human health and the environment. It should draw information from a wide range of credible sources and could also take into account expert advice of, and guidelines developed by, relevant international organizations. Effective communication and consultation with all interested parties should be ensured in all aspects and stages of the process of risk analysis.

## 2.3 THE METHODOLOGY OF RISK ASSESSMENT AND RISK MANAGEMENT: KEY STEPS

**METHODOLOGY OF RISK ANALYSIS**
Key steps of the process include: hazard analysis, likelihood estimation, consequence estimation, risk estimation, and risk management.

General guidance on the **methodology of risk assessment and risk management of GMOs** exists and they share many similarities. Annex III 8 of the Cartagena Protocol on Biosafety (CBD, 2000) is a good exemplary guide and the steps typically followed are enumerated below.

- Hazard analysis - An identification of any novel genotypic and phenotypic characteristics associated with the living modified organism that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health.
- Likelihood estimation - An evaluation of the likelihood of these adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the living modified organism.

- Consequence evaluation - An evaluation of the consequences should these adverse effects be realized.
- Risk estimation - An estimation of the risk posed by the living modified organism based on the evaluation of the likelihood and consequences of the identified adverse effects being realized.
- Risk management – A recommendation as to whether or not the overall risks are acceptable or manageable, including, where necessary, identification of strategies to manage these risks, including monitoring.

It should be noted that the level of details and sequence of some of the steps indicated above vary across countries. More detailed discussions of the methodology of risk assessment and risk management are presented in later chapters (see Chapters 3 and 4).

## 2.4 CONCEPTS AND ISSUES IN RISK ANALYSIS

There are a number of concepts and issues that are very important in gaining a better understanding of the process of risk analysis. These include:

### 2.4.1 The concept of familiarity

**FAMILIARITY**
Evaluating the potential risks of a GMO by comparing it with its non-modified counterpart.

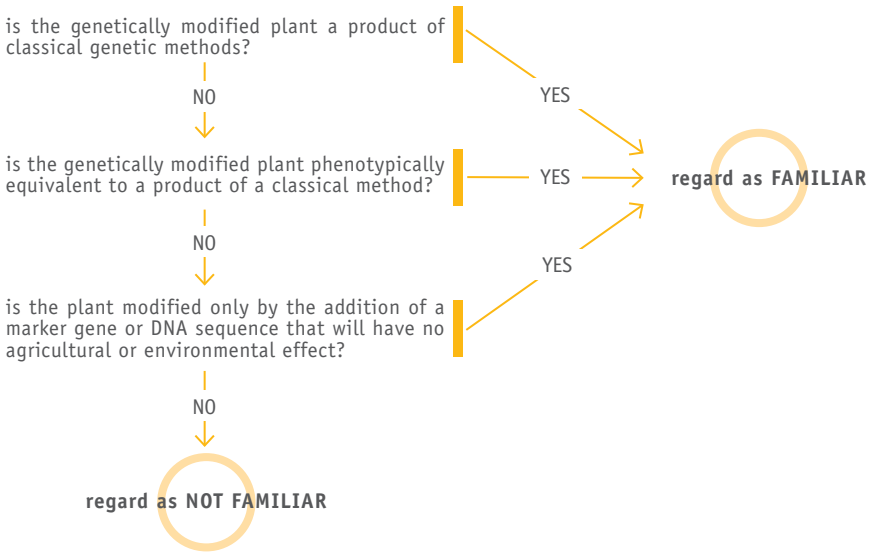
Risk assessment of GMOs requires information on the identity, characteristics and history of safe use of the organism that is subjected to genetic modification. Most GMOs to date have been developed from organisms that are "familiar" i.e. there is sufficient information available about the organism's attributes, and a long history and experience of its safe use.

The concept of familiarity provides a way to recognize the potential risks by using already available information on the attributes of the organism. Because of familiarity, effective methods can de devised to avoid or manage the risks

to acceptable levels. For example, it is possible to determine the potential for invasiveness of a GM crop based on knowledge of the biology of the non-modified organism (e.g. presence of traits that are associated with invasiveness) and the presence of wild compatible relatives. Likewise, it is possible to identify the potential allergenicity of a GMO if knowledge and history of safe use of the origin/source of the gene used in genetic modification is available. In this context, the concept of familiarity is not a risk assessment in itself, but a useful tool for identifying, evaluating and managing risks.

An example of a familiarity test for genetically modified plants is shown in the following illustration (Persley *et al.*, 1993):

Figure 2.2 | **A familiarity assessment framework**



## 2.4.2 The concept of substantial equivalence

**SUBSTANTIAL EQUIVALENCE**
The principle that GMOs can be compared with their conventional counterparts that have an established history of safe use.

In assessing the risks posed by GMOs to human health and the environment, the concept of familiarity is used together with the concept of **substantial equivalence**. Substantial equivalence is based on the principle that GMOs can be compared with their **conventional counterparts** that have an established history of safe use (Codex Alimentarius Commission, 2003). The concept is used to identify the similarities and differences (including intended changes and unintended changes) between the GMO and its conventional counterpart to be able to determine if the GMO is "as safe as" or presents any new or greater risks than its conventional counterpart. The concept of substantial equivalence does not establish absolute levels of safety, but relative levels of safety.

**CONVENTIONAL COUNTERPART**
A related organism/variety of the GMO, its components and/or products for which there is experience of safety based on common use as food.

Internationally, the concept of substantial equivalence is recognized as one of the principles for environmental risk assessment by the Cartagena Protocol on Biosafety, and in food safety assessment by the Codex Alimentarius Commission. The relevant texts (in italics) are as follows:

**Cartagena Protocol on Biosafety (CBD, 2000)**

**Annex III 5 – Risk Assessment**

*Risks associated with living modified organisms* or products thereof, namely, processed materials that are of living modified organism origin, containing detectable novel combinations of replicable genetic material obtained through the use of modern biotechnology, *should be considered in the context of the risks posed by the non-modified recipients or parental organisms* in the likely potential receiving environment.

**Codex Alimentarius Commission Principles and Guidelines on Foods Derived from Biotechnology (Codex Alimentarius Commission, 2004), Section 3.10 – Principles:**

> Risk assessment includes a safety assessment (…) The safety assessment *should include a comparison between the food derived from modern biotechnology and its conventional counterpart focusing on determination of similarities and differences*. If a new or altered hazard, nutritional or other safety concern is identified by the safety assessment, the risk associated with it should be characterized to determine its relevance to human health.

It should be noted that the concept of substantial equivalence is considered a *starting* point for the safety assessment to structure the safety assessment procedure, and to focus on the identified differences that may require further testing. Its application is limited by the choice of an appropriate comparator and availability of sufficient scientific information relevant to the risk assessment. These points are illustrated in the three cases presented below.

- *GMOs that are shown to be substantially equivalent to the conventional counterparts* are regarded as being "as safe as" their counterpart. No further safety considerations other than those for the counterpart are necessary.
- *GMOs that are substantially equivalent to the conventional counterpart except for defined differences* need further safety assessment which should focus only on the defined differences. Typically, the defined differences will result from the intended effect of the genetic modification that may, or may not, change the endogenous traits, or produce new traits in the host organism.
- *GMOs that are not substantially equivalent to the conventional counterpart*. Up to now, and probably for the near future, there have been few examples of these GMOs. Nevertheless, it is conceivable that with future developments in biotechnology, these kinds of GMOs will be produced. In these cases, the concept of substantial equivalence cannot be applied.

As a final note, in addition to the limitations mentioned above, the use of the concept of substantial equivalence in risk assessment has been criticized as subjective, inconsistent and pseudo-scientific (Millstone *et al*. 1999). However,

despite its limitations and criticisms, there is wide recognition that the concept of substantial equivalence remains the most practical approach currently available to framing the risk assessment process.

### 2.4.3 The precautionary approach

**THE PRECAUTIONARY APPROACH**
"Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation."

**Principle 15 of the Rio Declaration on Environment and Development (UNCED, 1992) states that:**

"In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation."

There are a number of important points to keep in mind about Principle 15 of the Rio Declaration in conducting risk analysis.

- The term "precautionary approach" is specifically used to differentiate it from the legal connotation of the term "precautionary principle". The latter is compulsory or legally binding while the former may be binding in some cases but normally does not have the same force as a law (Recuerda, 2008). Because it is an "approach" and not a "principle", Principle 15 allows for discrimination between countries in applying the approach based on their capability, which a law or principle will not allow. Furthermore, Principle 15 allows other costs (e.g. social or economic) to be considered in order to be cost-effective in applying the approach. In view of these, the "precautionary approach" is viewed as softening of the "precautionary principle".
- The precautionary approach in the context of Principle 15 explains the idea that scientific uncertainty (i.e. source or form of doubt) should not prohibit using preventive measures to protect the environment; and use of "cost-effective" measures indicates that costs can be considered when applying the approach.

- Principle 15 identifies the triggers to propose a precautionary approach.
- Finally, Principle 15 refers to potentially irreversible harm to be the most important application of the precautionary approach. Where risks for irreversible damage is high, decision-makers will act from the perspectives of prudence and precaution.

Many countries have adopted the same phrasing of Principle 15 of the Rio Declaration in their regulatory systems and have established risk assessment mechanisms based on the precautionary approach. The interpretation and implementation of the precautionary approach vary across countries because they differ in their opinions on thresholds of risk and degree of scientific uncertainty allowed in the process of risk analysis. Many regulatory approaches recognize the imperfect nature of evidence when making decisions. In conformity with the precautionary approach, preventive measures are built in their risk management design to allow certain activities with limitations, when appropriate.

### 2.4.4 Uncertainty

**UNCERTAINTY**
An inherent property of risk and present in all aspects of risk analysis, including risk assessment, risk management and risk communication.

Uncertainty is an inherent property of risk and is present in all aspects of risk analysis, including risk assessment, risk management and risk communication (Hayes, 2001). Simply defined, uncertainty is a form of source of doubt. There are five different types of uncertainty that can be applied to risk analysis, which are enumerated below:

- *epistemic* - uncertainty of knowledge, its acquisition and validation. The most common examples are statistical errors, use of surrogate data (e.g. extrapolation from animal models to humans), and incomplete, ambiguous, contested or unreliable data. Epistemic uncertainty could be reduced by designing more rigorous experiments, and by applying more powerful statistical analyses and GLP.
- *descriptive* - uncertainty of descriptions that may be in the form of words (linguistic uncertainty), models, figures, pictures or symbols (such as those used

in formal logic, geometry and mathematics). Usually associated with qualitative measurements and inconsistent and incomplete definition and application of words. For example, the word "low" may be ambiguously applied to likelihood of harm, magnitude of a harmful outcome and to the overall estimate of risk. Descriptive uncertainty could be reduced by using accurate and consistent definitions and providing clear parameters, scope and boundaries.

- *cognitive* (including bias, perception and sensory uncertainty) - cognitive uncertainty can be viewed as guesswork, speculation, wishful thinking, arbitrariness, doubt, or changeability. One way to reduce cognitive uncertainty is through effective communication strategies.
- *entropic (complexity)* - uncertainty that is associated with the complex nature of dynamic systems such as a cell, an organism, the ecosystem, or physical systems (e.g. the atmosphere). Complexity and incomplete knowledge contribute to the inability to establish the complete causal pathways in a system. Consequently, a deterministic system can have unpredictable outcomes because the initial conditions cannot be perfectly specified. Complexity could be reduced by generating more information about the various components and relationships in the system.
- *intrinsic* - uncertainty that expresses the inherent randomness, variability or indeterminacy of a thing, quality or process. Randomness can arise, for example, from genetic difference. A critical feature of intrinsic uncertainty is that it cannot be reduced by more effort, such as more data or more accurate data. In risk management, safety factors and other protective measures are used to cover this type of uncertainty.

There are a number of ways to address uncertainty in risk analysis of GMOs:

- Request or obtain further information on the specific issues of concern. Where there is uncertainty, more experiments may be required in order to answer the question. However, it must be recognized that the effort and resources required to acquire greater knowledge increase almost exponentially with each demand

BOX 2.1

## EXAMPLES OF UNCERTAINTY WITHIN THE ELEMENTS OF RISK ANALYSIS

**Risk assessment**

- Uncertainty in the nature of the GMO, such as the lack of knowledge of biochemical properties of the introduced genes, environment-specific performance of the GMO, its interaction with other biological entities and processes, or landscape changes over long time periods;
- Uncertainty of the calculations within the risk assessment process, including assessment of hazards, likelihood and consequences;
- Uncertainty in descriptions used in qualitative risk assessments due to insufficient explanations of terminology, use of related terms that are not fully congruent or the use of the same term in different contexts.

**Risk management**

- Balancing the sufficiency of protective measures against their effectiveness;
- Decision-making in the presence of incomplete knowledge and conflicting values.

**Risk communication**

- Uncertainty of communication effectiveness due to difference in knowledge, language, culture, traditions, morals, values and beliefs.

*Adapted from*: Australian Government, 2005.

for greater precision or detail. In many instances, these may not be technically (e.g. no valid protocol) or practically (e.g. unaffordable cost) possible.

- Implement appropriate risk management strategies and/or monitor the GMO in the receiving environment.
- In cases where further experimentation may not provide the necessary information, the "worst case" scenario approach can be applied, where the focus is less on determining the likelihood of an occurrence, but rather on evaluating what the consequences of the occurrence would be.

CHAPTER 3

# THE RISK ANALYSIS PROCESS: RISK ASSESSMENT

**COMPONENTS OF RISK ASSESSMENT**
(1) hazard analysis (hazard identification and characterization), (2) likelihood estimation, (3) consequence evaluation; and (4) risk estimation.

Risk assessment is the core of biosafety because it represents the basis for making decisions on the protection of the environment and human health in the case of uncertain scientific backgrounds. To guarantee its integrity and objectivity, risk assessment has to be separated from risk management.

**Risk assessment** is a science-based process consisting of four steps: (1) hazard analysis (hazard identification and characterization), (2) likelihood estimation, (3) consequence evaluation; and (4) risk estimation, all of which are described below.

A generally accepted methodology for biotechnology risk assessment has been outlined in several easily accessible documents including the UNEP International Technical Guidelines for Safety in Biotechnology (UNEP, 1995), the EC Directive 2001/18/EEC, and Annex III 8 (a-d) of the Cartagena Protocol on Biosafey (CBD, 2000). In this section, the latter is used as a guide to enumerate the steps typically

followed in risk assessment whether for food products or organisms released into the environment. The additional information to help explain each step was abstracted primarily from the Risk Analysis Framework of the Australian Government (2005) and the FAO Biosecurity Toolkit (2007).

## 3.1 KEY STEPS IN RISK ASSESSMENT

### 3.1.1 Hazard analysis, identification and characterization

**HAZARD ANALYSIS, IDENTIFICATION AND CHARACTERIZATION**
An identification of any novel genotypic and phenotypic characteristics associated with the living modified organism that may have adverse effects on biological diversity in the likely potential receiving environment.

Hazard analysis can be defined as an identification of any novel genotypic and phenotypic characteristics associated with the living modified organism that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health (CPB, Annex III 8 (a)).

Hazard identification investigates the intrinsic or "built-in" potential of the biological agent (e.g. GMO or GM foods) to cause harm. Hazard characterization aims to evaluate, in qualitative and quantitative terms, the nature of the identified intrinsic hazard. Quantitative and qualitative techniques are used in hazard identification (Hayes *et al*, 2001). Qualitative techniques include checklist, brainstorming, expert consultation, fault and event trees. Quantitative techniques include HAZOP analysis, hierarchical holographic model (HHM), SWOT analysis, Delphi analysis, etc. Approaches to hazard analysis may be inductive (top down) or deductive (bottom up). A checklist and the inductive approach appear to be the status quo of hazard analysis. Evidentiary support could range from unsubstantiated statements (weak evidence) to experimental data (strong evidence).

Hazard analysis also involves establishing the causal link and pathway or route of exposure between a hazard and an adverse outcome. It also involves identifying the measurable properties of the hazard in order to accurately assess that harm has occurred. Table 3.1 summarizes examples of potential biological harms and the respective measureable properties.

Table 3.1 | **Examples of potential harms and their measurable properties**

| Hazard | Measurement Attributes |
|---|---|
| Increased fitness, increased persistence, invasion of a GMO | Occurrence and biological properties – traits for weediness and invasiveness |
| Toxicity of a GMO to non-target organisms | Mortality; survival; population morbidity, species richness |
| Habitat modification - altered bio/geo-chemical cycles | Carbon, nitrogen, phosphorus flux; frequency of floods, fire; pollutant concentration |
| Loss of biodiversity and extinction of species | Diversity indices; species richness |
| Creation of new viruses | Occurrence, number, severity, host range |
| Human toxicity and allergenicity | Biological, physiological and physical abnormalities; mortality; frequency and age of morbidity |

## 3.1.2 Likelihood estimation

**LIKELIHOOD ESTIMATION**
An evaluation of the likelihood of adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the living modified organism.

Likelihood estimation can be defined as an evaluation of the likelihood of adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the living modified organism (CPB, Annex III 8 (b)).

Likelihood is the probability that the harm will occur. It is expressed as a relative measure of frequency (the number of occurrences per unit time) and probability (from zero to one, where zero is an impossible outcome and one is a certain outcome). It is important to remember that likelihood estimation is a predictive process. The accuracy of prediction is directly proportional to time of occurrence, i.e. a short-term outcome is more accurately assessed than a long-term outcome.

Here the term “estimation” is chosen because exact numbers of the frequency with which something will happen in nature cannot always be measured or predicted. It is possible in certain risk calculations, such as non-target risks, but more frequently the risk finding is qualitative on the basis of a weight of evidence analysis.

Likelihood assessment may be qualitatively described as follows:

- *Highly likely* - is expected to occur in most circumstances
- *Likely* - could occur in many circumstances
- *Unlikely* - could occur in some circumstances
- *Highly unlikely* (negligible or effectively zero) - may occur only in very rare circumstances

For GMOs, the most important factors that contribute to the likelihood that harm will occur are the survival, reproduction and persistence rates of the GMO, and the characteristics of the receiving environment, including its biotic and abiotic attributes.

### 3.1.3 Consequence evaluation

**CONSEQUENCE EVALUATION**
An evaluation of the consequences should adverse effects be realized.

Consequence evaluation is an evaluation of the consequences should adverse effects be realized (CPB, Annex III 8 (c)). Consequence evaluation involves characterizing the significance and impact of the adverse outcome if the hazard occurs. The following criteria should be taken into consideration:

- severity – number, magnitude, scale;
- spatial extent – geographical (local, national, global); organism (individual, population, community, ecosystem);
- temporal extent – duration and frequency;
- cumulation and reversibility;
- background risk – risk that may occur in the absence of the stressor (e.g. GMO).

Descriptors of consequence assessment:

- *Marginal* **-** minimal or no injury except to a few individuals who may require medical aid; minimal or no degradation of the environment;
- *Minor* **-** slight injury to some people who may require medical treatment;

disruption to biological communities that is reversible and limited in time and space or number of individuals/populations affected;

- *Intermediate* - injury to some people who require significant medical treatment; disruption to biological communities that is widespread but reversible or of limited severity;
- *Major* - Severe injury to some people who may require hospitalization or may result in death; extensive biological and physical disruption of whole ecosystems, communities or an entire species that persists over time or is not readily reversible.

### 3.1.4 Risk estimation

**RISK ESTIMATION**
An estimation of the risk posed by the living modified organism based on the evaluation of the likelihood and consequences of the identified adverse effects being realized.

Risk estimation is an estimation of the risk posed by the living modified organism based on the evaluation of the likelihood and consequences of the identified adverse effects being realized (CPB, Annex III 8 (d)).

Risk estimation combines the information on likelihood and consequence of the identified hazard to come up with the risk estimate matrix shown below (Figure 3.1). As a general rule, risks with moderate and high estimates will invoke the corresponding risk management treatments or control measures.

Descriptors of risk estimate:

- *Negligible* - risk is insubstantial and there is no present need to invoke actions for mitigation;
- *Low* - risk is minimal, but may invoke actions for mitigation beyond normal practices;
- *Moderate* - risk is of marked concern that will necessitate actions for mitigation that need to be demonstrated as effective;
- *High* - risk is unacceptable unless actions for mitigation are highly feasible and effective.

Figure 3.1 | **The combinations between severity and probability of a hazard and the resulting risk level classification**

| | | | PROBABILITY | | | | |
|---|---|---|---|---|---|---|---|
| | | | frequent | likely | occasional | seldom | unlikely |
| | | | A | B | C | D | E |
| SEVERITY | catastophic | I | extremely high | | | | |
| | critical | II | | high | | | |
| | moderate | III | | medium | | | |
| | negligible | IV | | low | | | |
| | | | RISK LEVEL | | | | |

*Adapted from*: Australian Government, 2005.

Finally, in conducting the steps outlined above, the following characteristics, depending on the dealing of GMOs, could be taken into consideration:

- recipient, host or parental organisms;
- inserted genes, sequences and related information about the donor(s) and the transformation system;
- the resulting GMO;
- available methods for detection and identification of the GMO;
- the intended use (e.g. the scale of the activity - field trial or commercial use);
- the receiving environment.

## 3.2 INFORMATION REQUIREMENTS FOR RISK ASSESSMENT

Risk assessment for the release of GMOs typically takes into consideration the points enumerated above obtained from Annex 9 of the Cartagena Protocol on Biosafety. A more detailed discussion of the various points is presented below (Konig *et al.*, 2002).

### 3.2.1 Information on the recipient or parent organism

**INFORMATION ON THE RECIPIENT OR PARENT ORGANISM**
Includes identity, agronomic performance, geographic distribution, history of safe use, compositional analysis, etc.

The type of information on the parent crop that should be gathered at the outset include:

- *Identity, phenotypic and agronomic performance* – taxonomic identity (including the complete name, family name, genus, species, subspecies, cultivar/breed/race/isolate, common name, and sexually compatible wild relatives); chemical proximate composition and key nutrients and anti-nutrients.
- *Geographical distribution/source or origin* – area of cultivation, centre of origin and centre of diversity.
- *History of safe use* – any known nutritional, antinutritional, toxicological, allergenic characteristics or intolerances; importance in the diet, including information on preparation, processing, and cooking.
- *Compositional analysis* – key nutrients, toxins, allergens, antinutrients, biologically active substances associated with parent and sexually compatible relatives; information both from the literature and from analytical data.

The recipient or parent organism refers to the organism into which the genes are introduced through genetic modification methods. The characteristics of the recipient organism guide the choice of test parameters for comparison of the GMO with its non-modified counterpart, i.e. it serves as a reference point. Knowledge of the natural variation of the traits in the recipient is essential in interpreting data when comparing the GMO with its non-modified counterpart under different receiving environments. The history of safe use of the parent can provide additional information to help plan the risk assessment strategy, e.g. identifying what should be the focus of further assessments.

The OECD has been compiling consensus documents (OECD, 2009) on the (1) biological attributes and (2) compositional characteristics for certain crop species. These documents provide excellent sources of relevant information on

the parent or recipient crop. Information from these OECD consensus documents has been accepted by biosafety regulatory authorities in some countries.

### 3.2.2 Information on the inserted genes and sequences and related information about the donor(s) and the transformation system

**INFORMATION ON THE INSERTED GENES AND SEQUENCES**
Includes description of the donor, description of the vector, characterization of the inserted DNA and the insertion site.

The information required includes:

- *Description of donor(s)* – includes classification and taxonomy, evidence of potential toxicity, allergenicity or pathogenicity, history of use and exposure to the donor; and, where possible, function of any recombinant DNA sequences used in the transformation.
- *Description of vector DNA* – includes information on the source of all genetic elements used to construct and amplify the transformation vector, including coding sequences, promoters and termination signals, vector maps with relevant restriction sites; proof of absence of vector fragments not intended to be transferred, and nucleotide sequence information.
- *Transgene delivery process* – For *Agrobacterium*-mediated transformation the information requirement includes donor strain and any plasmid contained in that strain; for direct transformation methods, such as the particle gun, it includes proof of absence of contaminating sequences of bacterial chromosomal DNA or other plasmid DNA or vector sequences.
- *Characterization of introduced DNA* – includes information on the number of insertion sites, copy number of the introduced DNA, ends of inserts adjacent to host genomic DNA; a genomic library of each transformed plant line (under discussion), absence of vector backbone; and verification of the stability of transgene insertion over five or more generations.
- *Characterization of insertion site* – information on the junction of the inserted recombinant DNA and the host genome.

With regard to the transformation method, it has been argued that in using *Agrobacterium,* the risk of transfer of random DNA to the plant is relatively small (Gelvin, 2000). The vector with the recombinant DNA may be separate from the vector with transfer function and contain a recognition site for the transfer-mediating gene products, thus limiting the chance of transferring transfer vector DNA.

With regard to the characteristics of the introduced DNA, all inserted *functional genes* are, in principle, relevant to the risk assessment, regardless of whether they are the "genes of interest" or genes that have "travelled along" in the process, such as selectable marker genes. The underlying reason is the possibility of unintended effects due to the presence of these DNA sequences. For example, a gene with a prokaryotic origin of replication (*ori*) will not be expressed in a plant cell, but will be considered in the risk assessment because it may facilitate replication of the gene in the – unlikely – event that it is taken up and recovered in a bacterium. To conclude, all regulatory regions and other sequences that are transferred to an organism in addition to the functional genes need to be included in the risk assessment.

Finally, the level of detail required should depend on the nature of the dealing. For example, in the early stages of research and development of the GM product, when full molecular characterization has not yet been conducted, it can be assumed that the entire construct may have been integrated into the recipient organism. Hence, the risk assessment is conducted on that basis and risk is managed by strict containment measures (see Section 2). When the activity has moved on to confined field trials, more detailed characterization is requested, leading to a full characterization as required for large-scale field trials or commercial/ market release. This is part of the "case-by-case" and "step-by-step" approach of risk analysis.

### 3.2.3 Information on the gene products; recombinant proteins and/or metabolites

**INFORMATION ON THE GENE PRODUCTS**
Includes characterization of proteins, mode of action, toxicity, allerginicity, etc.

With certain exceptions, like anti-sense DNA, all inserted functional genes transferred to the recipient organism are translated into primary (protein) and secondary (metabolite) gene products. Hence, both are relevant to the risk assessment process. The information required for the gene products is:

- *Structure, identity and characterization* – For proteins, this includes the molecular weight, amino acid sequence, post-translational modification (e.g. level of glycosylation and phosphorylation), immuno-equivalence, activity and specificity of catalysed reactions (if the gene product is an enzyme), expression levels (recombinant protein levels in various host tissues), changes in levels of inherent crop micro or macronutrients (e.g. Vitamin A in Golden Rice), and significant unexpected changes in the levels of substances detected during compositional analysis.
- *Mode of action/specificity* - mechanism of action (e.g. Bt-proteins which are toxic to certain insects but not humans), overview of all relevant metabolic pathways that could be affected by the enzyme's presence or altered levels or substance specificity (e.g. the CP4 EPSPS enzyme that confers tolerance to the herbicide glyphosate but does not affect the biosynthesis of the aromatic amino acids of all plants and micro-organisms).
- *Toxicity* – information on documented exposure and history of safe use; results of previous toxicity testing programmes; for novel proteins/metabolites, information on structure and function and toxicity tests are required.
- *Allergenicity* – changes in the characteristics or levels of expression of endogenous allergenic proteins, and/or allergenicity of the recombinant protein itself.

**TOXICITY AND ALLERGINICITY**
The primary concerns and focus of risk assessment, particularly for GMOs that will be used as food/feed.

**Toxicity and allergenicity** of the gene products are the primary concerns and focus of risk assessment, particularly for GMOs that will be used as food/feed. From the perspective of food/feed safety, it is widely recognized that proteins are not generally toxic when consumed orally as they are largely part of a standard human and animal diet. However, almost all allergens are proteins. With regard to toxicity, safety concerns

and the amount of new data that will be required should be carefully considered in the light of existing information on the protein/metabolite prevalence, similarity to proteins/metabolites that are routinely used by humans and animals, and history of exposure. Safety concerns and new data requirements should be lower in the case of proteins that have no history of adverse effects on humans and animals. With regard to allergenicity, the amount of new data required should take into account the following key considerations: (a) Is the recombinant protein derived from an allergenic source or known allergen? Is it able to induce *de novo* sensitization?; Is it cross-reactive with IgE antibodies raised by known allergens?; (b) Has transformation altered the allergenic properties of the product derived from the GMO?

### 3.2.4 Information on the resulting GMO

**INFORMATION ON THE RESULTING GMO**
Includes identity, agronomic analysis, compositional analysis, and safety analysis.

Information requirement for the resulting GMO includes:
(1) identity, phenotypic and agronomic analysis;
(2) compositional analysis and
(3) safety analysis (animal studies). The information from these analyses is obtained in comparison with the non-GM counterpart. These analyses focus on detecting any indicative differences in test parameters, such as agronomic performance, compositional and nutritional values, and dietary subchronic responses in animal feeding studies.

Sources of data to enable detailed comparison can come from a variety of sources. Data about the resulting GMO are available from growing the GMO in growth chambers, greenhouses and/or earlier field trials. Field trials are usually undertaken under a diversity of environmental conditions representative of those typical for planned commercial growing. Other major sources of data are databases on existing food composition, chemical analyses, and toxicology tests. Data can also be obtained from the Biosafety Clearing House for information on field and commercial releases of identical GMOs in various locations.

**GMO Detection and identification methods** are important in hazard identification and characterization. In various stages of research, development and release of a GMO, molecular characterization and toxicological tests are conducted to generate information on the characteristics of the inserted DNA sequences, the gene products, and the resulting GMO. This means that detection, identification and test methods focusing on the inserted DNA, the resulting proteins and the resulting GMO are crucial for GMO analysis.

**GMO DETECTION AND IDENTIFICATION METHODS**
Highly important for hazard identification and characterization; described in detail in Module A.

Examples of currently available DNA-based GMO detection methods widely used include:

- Southern blot
- Qualitative PCR
- Quantitative real-time PCR
- DNA chips

Protein-based testing methods include:

- Western blot
- ELISA
- Lateral flow strips
- Protein chips

Toxicology test methods include:

- i*n vivo* and *in vitro* test systems
- chronic toxicity, carcinogenicity and reproduction studies
- acute animal toxicity studies

Each of these methods has its own advantages and disadvantages in terms of targets, ease of use, specificity, sensitivity, costs, etc. Existing methods have proven to be adequate for the safety assessment of the GMOs that are currently available on the market. Development in the areas of detection and testing are being pursued

to improve existing techniques and address the safety of next generation products of modern biotechnology.

For a more detailed discussion on DNA and protein detection techniques, please refer to Module 1: Agricultural Biotechnology.

### 3.2.5 Information relating to the intended use of a GMO

**INFORMATION RELATING TO THE INTENDED USE OF A GMO**
This may include a wide range of activities, from basic research to large-scale commercial release.

The intended use of a GMO possibly encompasses a wide range of activities and applications. These include: (a) make, develop, produce or manufacture GMOs; (b) conduct experiments with GMOs; (c) breed GMOs; (d) propagate GMOs; (e) investigate the use of GMOs in the course of development or manufacture of a product; and (f) grow, raise or culture GMOs, possibly on an industrial scale.

These activities and applications can be classified into two categories: (1) contained use; and (2) release into the environment. Contained use means any operation undertaken within a facility, installation or other physical structure, which involves living modified organisms that are controlled by specific measures that effectively limit their contact with, and their impact on, the external environment (CPB definition).

Release into the environment, in this document, refers to non-contained usage of GMOs. In many regulatory systems, this means any trial conducted in the field irrespective of scale and availability of confinement measures and commercial release. The major distinction between commercial release and field trials is that with field trials the GMO involved is still under various degrees of control, whereas after placing the GMO on the market for commercial production, its use is, in principle, unrestricted except for specific product-use conditions, such as labelling or monitoring.

### 3.2.6 Information on the receiving environment

**INFORMATION ON THE RECEIVING ENVIRONMENT**
The characteristics of the receiving environment are crucial for the risk assessment.

The characteristics of the receiving environment are crucial for the risk assessment. When releasing genetically modified plants into the environment, there are relevant questions for specific applications to be assessed:

1. Is there potential for negative impact on managed ecosystems?
2. Does the GMO have altered resistance to insects or pathogens?
3. Does the GMO have new weed characteristics?
4. Does the GMO pose hazards to local fauna or flora?
5. Is there potential for negative impact on natural (non-managed) ecosystems?
6. Are cross-hybridizing relatives present in the same area?
7. Can the new trait impart increased competitiveness to weedy relatives?
8. Does the GMO have new weed characteristics that could make it successful outside of the managed ecosystems?

For field trials, the information requirement includes the specific physical location of the trial, taking into consideration the following relevant characteristics:

- comparison between the normal growing environment with the proposed environment for release;
- specific environmental factors influencing survival and distribution of the organism (e.g. climate, soil conditions);
- presence of sexually compatible crops;
- presence of sexually compatible wild relatives.

Taken together, it should be clear that risk assessment is a complex, science-driven process, that needs to integrate a variety of data and considerations. Since every GMO is different concerning its design, purpose, biology of the parent organism and the likely receiving environment, risk assessment has to be performed on a case-by-case basis for each individual GMO case. In Annex 4, a summary of points to be taken into consideration for the risk assessment of GMOs, extracted from European Community (EC) legislation, is provided as an additional guideline.

CHAPTER 4

# THE RISK ANALYSIS PROCESS: RISK MANAGEMENT

**RISK MANAGEMENT**
The process of weighing policy alternatives to mitigate risks in the light of risk assessment, and, if required, selecting and implementing appropriate control options, including regulatory measures.

Risk management is the second and the decision-making component of the process of risk analysis. **Risk management** is defined as "the process of weighing policy alternatives to mitigate risks in the light of risk assessment, and, if required, selecting and implementing appropriate control options, including regulatory measures" (FAO/WHO, 1995). Its objective is to determine which risks require management and how these risks can be effectively managed or controlled so that the goal of ensuring adequate protection for people and the environment is attained.

The management of risk is basically founded on:

- Understanding and identification of risks and adverse conditions associated with work, which are determined in the risk assessment process. The principal objective of the evaluation is to know which management measures and controls are to be applied to the identified risks. If a risk is not identified, one cannot develop risk management procedures.
- The development and implementation of technical and organizational measures that correspond with the determined risks.
- The type of organism released (transgenic, non-transgenic, exotic).

The risk management framework is depicted in Figure 4.1:

Figure 4.1 | **Components of a generic risk management framework**


*Adapted from*: FAO, 2007.

The fundamental **objective of the risk management** process is to:

- eliminate, reduce or substitute the risk factors identified in the risk assessment;
- avoid or reduce exposure to the identified risk factors.

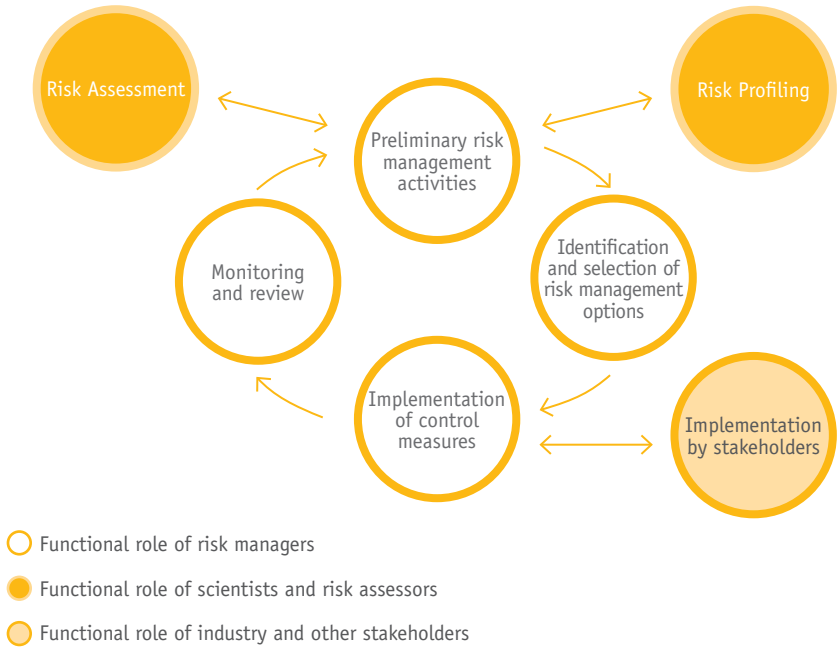
**OBJECTIVE OF RISK MANAGEMENT**
Eliminate, reduce or substitute the risk factors identified in the risk assessment; and avoid or reduce exposure to the identified risk factors.

As such, the measures to develop could be those for:

- elimination of risks;
- reduction of risks;
- substitution of risks.

Although other stakeholders participate in risk analysis, at a national level it is the competent authority having jurisdictional power that makes the final risk management decisions and has the overall responsibility for ensuring that control measures are properly implemented and complied with. The relations between risk managers, scientists and risk assessors and other stakeholders is depicted in Figure 4.2:

Figure 4.2 | **Role of the risk manager in application of the generic risk management process**




*Adapted from*: FAO, 2007.

The preliminary risk management activities can indicate that:

- The available information is sufficient and the competent authority can therefore be authorized to evaluate the risks.
- The available information is not adequate and it is therefore necessary to request more information.
- The case is straightforward or there already exists adequate experience and information on risks and the required biosafety measures, and the formal risk evaluation can begin.

If the risk evaluation is commissioned, the competent authority should clearly and objectively formulate the scope of the risk evaluation and the questions to be addressed.

Risk management measures are various; they can be simple or a combination of different measures, contributing to more complex management. The general procedures are those applicable to all organisms (transgenic or non-transgenic) before their use and release into the environment according to technical and engineering measures, including control techniques and organizational measures. Specific measures depend on the type of organism.

In any case, risk management is primarily supported by the results of the risk assessment process but may consider risks in a wider context. This allows the risk manager or designated national competent authorities to take into consideration other inputs, e.g. socio-economic considerations (if allowed by the regulation) from other interested parties concerned with risks, in the final decision on any dealing of GMOs. This adds a political component to the risk management process.

There is a general consensus that, in order to maintain the scientific integrity of the risk assessment process, it is important to keep the conceptual separation between risk assessment and risk management.

**KEY STEPS IN RISK MANAGEMENT**
Include risk evaluation, risk mitigation, and implementing appropriate actions.

## 4.1 THE KEY STEPS IN RISK MANAGEMENT

Risk management is a step-by-step process which consists of:

### 4.1.1 Risk evaluation

In this step, decisions are made on whether the identified risk is manageable, i.e. a consideration of appropriate risk management strategies.

**RISK EVALUATION**
In this step, decisions are made on whether the identified risk is manageable, i.e. a consideration of appropriate risk management strategies.

The rigorous scientific process of the risk assessment implementation ends in a risk estimate. Risk evaluation starts from the result of the risk estimation step. In cases where, on the basis of the risk estimation step, the risks involved are not deemed to be "negligible" or "marginal", the risk evaluation considers whether the identified risk is manageable or acceptable. The question to address is whether the identified risks require specific risk management measures. If the answer is "yes", then a risk management strategy is defined in the next step. For example, risks with estimates of high or moderate would generally invoke a requirement for management.

Risk evaluation serves as the vital link between risk assessment and risk management. In practice, the functional separation between risk management and risk assessment is less clear in this step.

### 4.1.2 Risk mitigation

**RISK MITIGATION**
Determines the options and plans to reduce or avoid the risks.

This step is central to the risk management process. It determines the options and plans to reduce or avoid the risks. For cases where a risk management strategy has been defined, the risk assessment "loops back" to the earlier steps in the risk assessment to determine whether the proposed risk management strategies sufficiently reduce the likelihood or the consequence of potential adverse effects.. This is one reason why risk assessment is often called an "iterative process". Availability of new data, derived for instance from a confined, "risk managed" field experiment, may also be a reason to revisit and possibly revise a risk assessment.

Depending on the case, risk mitigation measures or options may include:

» specifying the appropriate containment facilities and BSLs (please see Chapter 2), as well as the conditions for use, handling, storage, transport and disposal of biological material. For genetically modified plants: reproductive isolation by removal of flowers, use of isolation distances or border rows, temporal

isolation, special design features such as male sterility, and reduction of the size or duration of an application can be considered and evaluated in:

  - Controlled field trials (isolated from other cultivated areas)
  - Semi-commercial tests (contained)
  - Commercial-scale tests (under field production conditions)
- submission of contingency or emergency plans
- monitoring and surveillance
- GMO detection (for details, please see Module 1)
- labelling (voluntary or mandatory)

BOX 4.1

## POST-COMMERCIALIZATION RISK MANAGEMENT THROUGH LABELLING AND MONITORING TECHNIQUES

Risk management can include the element of traceability in the case of GMOs and particularly in the case of transgenic foods. Traceability is the capacity to follow the organisms or their products in all the phases of commercialization, along the production and distribution chains, to control quality and when necessary recall materials. This is possible through labelling and monitoring techniques and can increase costs. Traceability does not only apply to GMOs, it applies to all foodstuffs.

As far as the objectives of post-commercialization are concerned, these include:

- Following the long-term effects on human health and the environment.
- Recalling products if there is a perceived risk to human health and the environment.
- Assisting control through labelling.
- Preservation of the identity of specific products.

*Detailed information on all aspects of monitoring, surveillance and emergency planning are presented in Module D.*

Many countries have put up their own guidelines for dealings on GMOs but there are still no internationally agreed guidelines, except for containment, on exactly how these risk management measures are designed and implemented. Efforts are under way to standardize and harmonize the guidelines on these various risk management measures.

### 4.1.3 Selecting and implementing the most appropriate options and actions

**SELECTING AND IMPLEMENTING OPTIONS AND ACTIONS**
The final decision-making process that will ultimately lead to authorization and issuance, or rejection, of the licence required for any dealing of GMOs.

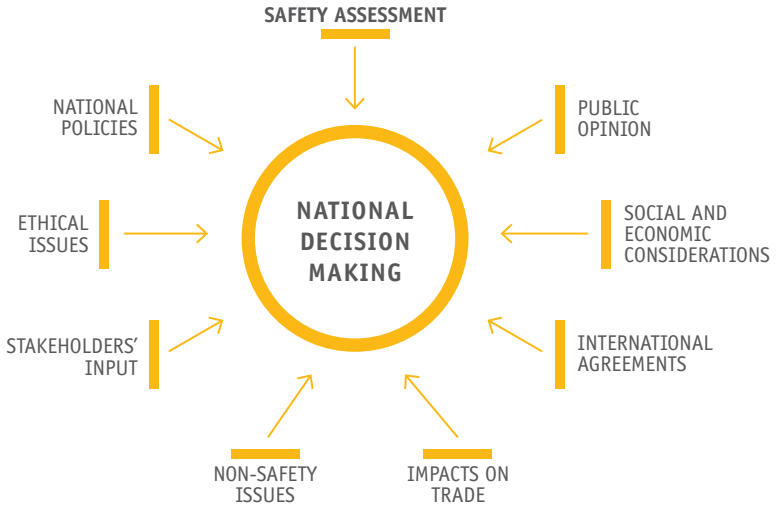
This step refers to the final decision-making process that will ultimately lead to authorization and issuance, or rejection, of the licence required for any dealing of GMOs. The risk mitigation measures identified are included as part of the licence conditions.

Final decisions are based primarily on the results of the scientific process of risk assessment. However, several factors govern decisions about the release of a GMO and in this step, the risk management process may take into account other non-risk issues (e.g. socio-economic considerations) and other risk-related factors (e.g. risk perceptions) from various stakeholders to inspire confidence and achieve wider acceptance of the decision. These stakeholders have diverse views and may have conflicting interests.

Decision-makers need to balance the individual rights of different stakeholders with the need to protect human health and the environment from the adverse effects of unacceptable risks. This step makes the risk management process essentially a political process.

Typically, decision-making incorporates, whether formally or informally, stakeholder input, public concerns and opinions, existing policies in agriculture, the environment, and food safety and responsibilities under international agreements. These factors are summarized in the following figure:

Figure 4.3 | **Factors influencing national GMO decision-making**




*Adapted from*: Traynor *et al.*, 2002.

Countries individually decide whether to develop, deploy, or use GMOs and the products made from them. Such decisions take into account national policies for agricultural research and development and the potential role of biotechnology in meeting national goals and objectives in food production, food security, trade and related areas. Decisions regarding the use of this technology and its products are based, in part, on a determination that they do not pose an unacceptable risk to the environment or to human health.

With the Cartagena Protocol on Biosafety, a legally binding international protocol for the safe transfer, handling and use of living modified organisms that is already in force, biosafety assessments will become part of international trade agreements.

## 4.2 RISK MANAGEMENT AND SOCIO-ECONOMIC CONSIDERATIONS

**SOCIO-ECONOMIC CONSIDERATIONS**
Such considerations might be taken into account during the risk management process.

**Socio-economic considerations** cover a wide range of issues and concerns. There are two relevant international documents which address socio-economic considerations in decision-making with regard to potential risks of GMOs to people and the environment. These are: (a) the Cartagena Protocol on Biosafety of the Convention on Biological Diversity; and (b) the Codex Alimentarius (international food code). Article 26 of the Cartagena Protocol on Biosafety, in particular paragraph 1 states that:

*1. The Parties, in reaching a decision on import under this Protocol or under its domestic measures implementing the Protocol, may take into account, consistent with their international obligations, socio-economic considerations arising from the impact of living modified organisms on the conservation and sustainable use of biological diversity, especially with regard to the value of biological diversity to indigenous and local communities.*

It is clear in Article 26 of the CPB that countries may take into account socio-economic considerations in making decisions with regard to GMOs. Paragraph 1 of Article 26 defines the limits and conditions when applying socio-economic considerations in decision-making on risks posed by GMOs to the environment. The definition implies that not all socio-economic considerations can be included, but only those where GMOs directly impact biodiversity. It also specifies the condition that when countries decide to take into account socio-economic considerations in decisions on GMOs, it must be done in a manner that is

consistent with other international obligations, which includes treaties of the World Trade Organization (WTO).

Codex Alimentarius guidance documents also state that socio-economic considerations may be taken into account in decisions on GMOs. Unlike the CPB, Codex principles are not legally binding to national legislations. However, Codex principles are referred to specifically in the Sanitary and Phytosanitary Agreement (SPS) of the WTO, which is a legally binding international treaty signed by many countries. (For details, please refer to Module E).

Codex principles on risk management particularly relevant to socio-economic considerations include Section 3.16 of Codex Alimentarius for foods derived from modern biotechnology (2003), which states that:

*"Risk management measures for foods derived from modern biotechnology should be proportional to the risk, based on the outcome of the risk assessment and, where relevant, taking into account other legitimate factors in accordance with the general decisions of the Codex Alimentarius Commission as well as the Codex Working Principles for Risk Analysis."*

Appendix IV of the Codex Working Principles for Risk Analysis on human health (Codex, 2003) and the Criteria for the Consideration of the Other Factors Referred to in the Second Statement of Principles outlines the points and criteria relevant to socio-economic considerations.

These include:

- other legitimate factors relevant for the health protection of consumers and for the promotion of fair practices in food trade based on the following criteria:
  - other factors should not affect the scientific basis of risk analysis
  - other factors which can be accepted on a worldwide basis, or on a regional basis

- specific other factors should be determined on a case by case basis
- other factors should consider the feasibility of risk management options and concerns related to economic interests and trade issues
- other factors should not create unjustified barriers to trade

The risk management process should:

- take into account an assessment of their potential advantages and disadvantages
- consider the economic consequences and feasibility of risk management options, paying particular attention to the circumstances of developing countries

As can be noted in the above, the existing guidance documents treat socio-economic considerations in general terms. To date, there are still no internationally agreed definitions and scopes of socio-economic considerations and methodologies for analysis and incorporating socio-economic considerations into the decision-making process. Even at the national level and for what may be considered a "legitimate factor" like economic risk-benefit analysis, there are no biosafety regulatory systems that have formally included a benefit assessment within their regulatory structure.

CHAPTER 5

# THE RISK ANALYSIS PROCESS: RISK COMMUNICATION

Risk communication is "the interactive exchange of information and opinions throughout the risk analysis process concerning hazards and risks, risk-related factors and risk perceptions among risk assessors, risk managers, consumers, industry, the academic community and other interested parties, including the explanation of risk assessment findings and the basis of risk management decisions" (Codex Alimentarius Commission, 2003).

**RISK COMMUNICATION**
The interactive exchange of information and opinions throughout the risk analysis process concerning hazards and risks, risk-related factors and risk perceptions among risk assessors, risk managers, consumers, industry, the academic community and other interested parties.

Risk communication in this sense is also addressed in Article 23 of the Cartagena Protocol on Biosafety on public awareness and public participation which states that:

1. *The Parties shall: (a) Promote and facilitate public awareness, education and participation concerning the safe transfer, handling and use of living modified organisms in relation to the conservation and sustainable use of biological diversity, taking also into account risks to human health. In doing so, the Parties shall cooperate, as appropriate, with other States and international bodies; (b) Endeavour to ensure that public awareness and education encompass access to information on living modified organisms identified in accordance with this Protocol that may be imported.*

2. *The Parties shall, in accordance with their respective laws and regulations, consult the public in the decision-making process regarding living modified organisms and shall make the results of such decisions available to the public, while respecting confidential information in accordance with Article 21.*
3. *Each Party shall endeavor to inform its public about the means of public access to the Biosafety Clearing-House.*

There is wide agreement that effective risk communication is essential at all phases of risk assessment and risk management. It is also recognized that risk communication involves not only risk assessors and risk managers, but also other interested parties like government, industry, academia, consumers, public interest groups and individuals concerned with risk.

Risk communication is essential in making decisions (ILGRA, 1999). It enables all interested parties, not only risk assessors and risk managers, to participate in deciding how risks should be managed.

Communication is also a vital part of implementing decisions - whether explaining mandatory regulations, informing and advising people about risks which they can control by themselves, or dissuading people from risky, antisocial behaviour. Therefore, the main goals of risk communication are: (1) to improve knowledge and understanding on all aspects of the risk analysis process by all interested parties concerned with risk; and (2) to promote interactive communication between risk assessors, risk managers and other interested parties concerned with risks in order to achieve the desired outcomes.

Risk does not have to turn into a crisis if it can be identified, planned for, and dealt with effectively. Good communication is the key. Good Risk Communication is the presentation of a *scientific assessment of risk* in such a way that the public can understand the information of the risk without becoming emotionally involved.

Good risk communication must:

- translate the scientific findings and probabilistic risk assessment into understandable terms;
- explain the uncertainty ranges, knowledge gaps, and ongoing research programmes;
- address issues of credibility and trust;
- understand the public's concern with regard to risk issues, and acknowledge their questions and concerns;
- analyze the conditions needed for the public to acquire relevant information, skills, and participatory opportunities.

**Good communication** with the public can also help responsible agencies to handle risk more effectively:

- **Lead to better decisions about how to handle risks**

  Considering and integrating a wide number of public and stakeholders' opinions may contribute to formulating well-suited and adequate decisions about the management of a certain risk.

- **Preventing crises**

  Early discussions with stakeholders and the public can help to inform responsible authorities of potential areas of public concern early on. This can enable them to take early action to address those concerns, before they turn into crises. It can be particularly valuable where there are public concerns about risks associated with new technologies, such as GMOs. Engaging a wide range of stakeholders and the public in risk decisions can help ensure that decisions take account of a wide range of views and experience. It can also help responsible authorities to spot aspects of a risk that might otherwise have gone unnoticed. This can be particularly important where action taken to tackle a risk could have a knock-on effect on others.

- **Smoother implementation**

  A key feature of risk management, and of policy-making, is the need to deal with

**GOOD COMMUNICATION**
Good communication with the public will profit the entire risk analysis process in a variety of ways, e.g. result in better decisions, prevent crises, build trust etc.

different and often conflicting perspectives. Engaging stakeholders and the public at an early stage in decisions about risks can help ensure that decisions better reflect public values and can reduce the scope for misunderstanding, disagreement and bitterness later on. This can make it easier to implement measures to address risks, particularly where these require the public to take action.

» **Empowering and reassuring the public**

Providing clear and accurate information about the nature of risks can help people to make realistic assessments of the risks they face and, where appropriate, to make informed judgments on how to handle risks by themselves. This can in turn help to foster a climate of greater empowerment and reassurance, and reduce the risk of scares.

» **Building trust**

Over time, communication with stakeholders can help to reduce suspicion, and build trust in the information government provides. Open communication can help by bringing people "inside the tent", and by enabling them to see for themselves that decisions have been made on the best available evidence and with the public interest in mind.

Also, effective risk communication can help responsible agencies to:

» explain technical risks more effectively;
» understand the multi-dimensionality of risk;
» anticipate community responses to the intended activities;
» respond to public concerns and misinformation;
» increase the effectiveness of risk management decisions by involving concerned community members;
» improve dialogue and reduce tension between communities and companies;
» build relationships based on trust and respect;
» develop a good reputation with regulators and the public;
» build a foundation for dialogue and shared problem solving before operations begin.

## 5.1 WHEN TO COMMUNICATE ABOUT RISK

It is widely acknowledged that risk communication is an integral part of the risk analysis process. It is embedded into the risk assessment and risk management processes; two key steps – hazard identification and selection of risk management measures – require effective risk communication to help build trust, reduce conflicts and achieve desired outcomes. In hazard identification, the views and opinions of interested parties about the potential hazards can help define the issues of concern and reduce potential points of conflict. During the selection of risk management options, the risk managers may need to consider factors in addition to the scientific input in the evaluation of a risk. This should involve active participation of stakeholders and other interested parties. Finding a common language that will be clearly understood by all parties is needed in explaining the results and the procedures of the risk assessment and risk management processes.

## 5.2 APPLYING RISK COMMUNICATION PRINCIPLES IN RISK ANALYSIS

**RISK COMMUNICATION PRINCIPLES**
Several elements, principles, barriers and strategies for effective risk communication have been identified.

The joint FAO/WHO expert consultation on the application of risk communication to food standards and safety matters identified the elements, principles, barriers and strategies for effective risk communication (FAO, 1999). The principles, applied to risk assessment and risk management processes, are illustrated below:

- *Know the audience*. In the risk analysis process, the different types of audience may include risk assessors, risk managers, government, interest groups and the general public. It is important to listen to and understand their motivations, opinions, concerns and feelings. These are important in the development and delivery of credible information on the risks identified, the decisions made, and the processes used. Understanding the audience's perception of risk can be done through surveys, interviews and focus groups.

- *Involve the scientific experts*. Scientific experts are primarily involved in the risk analysis process in their capacity as risk assessors. They work very closely with the risk managers in arriving at the final decision on any dealing with GMOs. These experts must be able to explain clearly the results of their assessment, including the assumptions and subjective judgments, so that risk managers can clearly and fully understand the risks and consequently formulate their decision.
- *Establish expertise in communication*. The risk analysis process generates enormous amounts of information which is of interest to a wide-ranging audience. Developing credible information and delivering it effectively requires communication expertise. Risk communication experts have to be involved as early as possible. Communication expertise of risk managers and risk assessors has to be improved by training and experience.
- *Be a credible source of information*. In the risk analysis process, the sources of information are risk assessors, risk managers, applicants of the technologies in question, and other interested parties. Information from a credible source will likely be accepted. For example, information from the Codex Alimentarius Commission on food safety assessments will more likely be accepted than information from a company consultant. Consistent messages from multiple sources lend more credibility to the risk assessment. Results of safety assessments by regulatory bodies of many countries on a particular GMO will likely receive higher acceptance. To be credible, the source of information should be perceived as genuinely concerned with the views and opinions on the risk issues, trustworthy, competent, committed and consistent. Timeliness in delivery and up-to-date information to address current issues and problems adds to the credibility of a source.
- *Share responsibility:* There are multiple actors involved in the risk analysis process. These include risk assessors, risk managers, other interested parties and the media. Each has a specific role to play, but have joint responsibility for the outcome. Since science must be the primary basis for decision-making,

all parties involved in the communication process should know the basic principles and data supporting the risk assessment and the policies underlying the resulting risk management decisions.

- *Differentiate between science and value judgment.:* It is essential to separate "facts" from "values" in reporting the results of the risk assessment and decisions made in the risk management process.
- *Assure transparency*. For the public to accept the risk analysis process and its outcomes, the process must be transparent. This means the process and results of risk assessment and risk management must be accessible and available for examination by interested parties, but giving due regard to confidentiality of information (if allowed by regulation).
- *Put the risk in perspective*. In the process of risk analysis, this can be done by emphasizing the information about the risk that is relevant to help the target audience make up its mind. For example, in the decision-making step, the risk manager may examine the risk in the context of the benefits associated with the technology. Risk comparisons that underestimate the concern should be avoided.

## 5.3 FACILITATING PUBLIC ENGAGEMENT IN THE RISK ANALYSIS PROCESS

Risk communication not only aims at informing and educating the public, i.e. improving the understanding of risk issues, but also at dealing with conflicting views and interests of the regulators, other interested parties and the general public on all aspects of the risk analysis process. Engaging all parties in a responsive and interactive dialogue may not change their individual positions, but may lead to a better understanding of and increased level of acceptance in the decisions made.

**FACILITATING PUBLIC ENGAGEMENT**
Engaging all parties in a responsive and interactive dialogue may lead to a better understanding and increased level of acceptance in the decisions made.

The need to engage the public in decision-making processes concerning the safety of GMOs to people and the environment is increasingly being recognized. This trend is

clearly presented in the results and background documents of the FAO Biotechnology Forum (Ruane and Sonnino, 2005). The decision-making processes identified where public engagement is needed are risk assessment and risk management, particularly in the approval of GM products. However, there are still no internationally agreed guidelines as to the extent and manner public input can be integrated into the risk analysis process.

The joint FAO/WHO expert consultation on application of risk communication to food standards and safety matters (FAO, 1999) identified steps in the risk analysis process where public input may be considered. The most important is the risk management step, specifically in the identification and weighting of policy and decision alternatives by risk managers. It was suggested that interested parties, whenever practical and reasonable, should be involved in identifying management options, developing criteria for selecting those options and providing input to the implementation and evaluation strategy.

The Institute for Development Studies (IDS, 2003) also considered some of the choices regarding the point at which the public could be involved in the decision-making process in the implementation of regulatory frameworks. In the context of the risk analysis process, some of the choices identified are:
(1) identification of risk issues (what do citizens know, what are they concerned about?); (2) roles, duties and powers of responsible agencies; (3) mechanisms of reporting, public scrutiny and accountability; (4) location and design of biosafety trials. The kinds of processes that then may be used include: (1) engaging with areas of public concern (rather than assuming what people need to know); (2) ensuring openness about applications for biosafety review and commercialization; (3) ensuring openness about the purpose, location and design of biosafety trials; (4) ensuring opportunities for public comment.

BOX 5.1

## ENGAGEMENT OF STAKEHOLDERS

**Questions that will assist in identifying relevant stakeholder groups**

- which branches of government(s) are officially involved in the applicable regulatory process?
- who might be affected by the risk management decision?
- who has information and expertise that might be helpful?
- who has been involved in similar risk situations before?
- who has expressed interest in being involved in similar decisions before?
- who reasonably might be angered if not included?

**Example of tactics to engage stakeholders**

MEETING TECHNIQUES

- public hearings
- public meetings
- briefings
- question and answer sessions
- focus groups
- workshops
- inclusion of non-scientific stakeholder groups in scientific meetings

NON-MEETING TECHNIQUES

- interviews
- hotlines and toll-free numbers

The kinds of tools which may be considered include stakeholder forums that are accessible and widely advertised and public registers of applications under review, with routine opportunities for public comment and obligations to respond to public comments. Furthermore, it should be noted that the perception of risk is highly subjective and context-dependent. Factors that may influence the public perception of risk, and which therefore need to be considered when engaging in communication with the public and establishing a dialogue on risks and risk analysis processes, include the following:

- **Dread.** Hazards that provoke a risk that is perceived as dreadful tend to evoke stronger fears than something seen as less dreadful.

- **Control.** When an individual feels as though she/he has some control over the process determining the risk faced, that risk usually seems smaller than if it had been decided by a process over which the individual had no control.
- **Natural** or human made. Natural risks (e.g. sun radiation) are usually perceived as less wonying than human-made risks (e.g. anthropogenic sources of radiation) even when facts show that the former present greater risks.
- **Choice.** A risk that an individual chooses usually seems less risky than a risk that is imposed.
- **Children.** Risks to children are generally perceived as worse than the same risk to adults.
- **Awareness.** Greater awareness of a risk increases conscious concern about that risk.
- **Personal exposure.** Any risk seems larger if an individual thinks they or someone they know could be a victim - this helps explain why statistical probability is often irrelevant to people and an ineffective form of risk communication.
- **Risk-benefits trade-off.** When people perceive a benefit from a certain behaviour or choice, the risk associated with it seems smaller (e.g. the benefits of a vaccination are perceived to outweigh the risk of the side effects); if there is no perceived benefit, the risk seems larger.
- **Trust.** Research has shown that the less people trust the institutions that are responsible for exposure to the risk or communication about the risk, the more they will be afraid.

As a final note, IDS emphasized that public participation is highly contextual. While the concerns are similar, there is no “one size fits all” formula for public participation and awareness-raising. What works in some places or in some circumstances will not work everywhere. Appropriate forms of public participation and consultation need to take into account the different situations, sociological differences, capabilities and stages of development of each country.

ANNEX 1

# MANAGEMENT OF RISKS IN FACILITIES

## A CAUSES OF ACCIDENTS IN LABORATORIES FOR BIOLOGICAL CONTAINMENT

Most **accidents** in containment facilities occur due to inadequately trained staff, poor handling, negligence and lack of adherence to norms of prevention and protection. For such reasons, national and international organizations, such as the WHO, have developed technical guides on general and specific methods that should be taken into consideration in facilities dealing with pathogenic agents.

**ACCIDENTS**
Most accidents in containment facilities occur due to inadequately trained staff, poor handling, negligence and lack of adherence to norms of prevention and protection.

The probability of accidents occurring when working with pathogens is directly related to the type of work being done, but is generally much lower in facilities in which the personnel are better trained. Training on the following topics should be provided:

- nature of dangerous agents, substances and products that exist in the laboratory;
- work procedures, the means of containment and safety and the means for individual protection;
- use and operation of equipment;
- means for disinfection and sterilization;
- what to do in the case of emergencies.

**CAUSES OF ACCIDENTS**
Generally, causes of accidents can be grouped into technical factors (equipment etc.) and subjective factors (personnel).

The **causes of accidents** in containment facilities are diverse. Therefore, an assessment of the potential risk has been developed to furnish norms and methods for adequate containment and protection for each type of laboratory and for each situation. To guarantee safety at work with pathogens or GMOs, two important factors should be considered:

- The objective or technical factors regarding the facility and its equipment, in terms of guaranteeing containment and safety.
- The subjective factors, in terms of the people who, in one form or another, are involved in the laboratory processes and who are important in carrying out the work under safe conditions.

Accidents result from circumstances where containment measures and equipment fail or where safety practices and procedures are not followed. Such situations can be caused by personnel obviating inconvenient procedures designed for their own safety and not applying correct containment procedures because of badly maintained equipment and facilities. Independent of their diverse nature, accidents can be grouped according to the factors that cause them:

- Technical factors normally associated with badly functioning equipment, methods and systems of protection, containment and biosafety.
- Subjective factors, related to poor use of equipment and methods, failure to observe technical procedures, poor control over processes, lack of attention, tiredness and other uncontrolled actions.

The causes of contamination can also be grouped by:

- Organizational causes, associated with supervising and overseeing work or the lack of a security procedure.
- Technical causes, associated with methods of protection, equipment functioning, operation of security systems, failure to adhere to GLP and factors concerning safety procedures.
- Human causes, associated with capacity, training and discipline, as well as psychological conditions.

Inherent risk factors associated with security at the facilities and during transport of the biological agents should also be taken into consideration. The possibility of entrance of non-authorized personnel or lax security during transport can jeopardize safety and result in liberation of biological material dangerous to humans, animals and plants.

Training and experience, state of health, prophylaxis and medical monitoring of exposed personnel are important. The general level of training in measures of prevention and protection, and specific work experience with the biological materials being handled, represent main factors in the prevention of accidents. When working at BSL 1, it is sufficient to know the GLP of the laboratory and have general experience in necessary techniques. However, from level 2, and particularly at level 3 and 4, it is necessary to have in-depth training in biosafety and specific experience in working with the samples.

The state of health of the personnel is one of the most important factors to be taken into account in assessing risk. All conditions that might predispose personnel to transmissible infections must be considered, including pregnancy or lactation. In this respect, regular medical monitoring of personnel and adequate prophylaxis must be instituted.

## B OTHER RISKS IN FACILITIES: CHEMICAL, PHYSICAL AND PSYCHO-PHYSIOLOGICAL

### B.1 Chemical risks

**CHEMICAL RISK**
Risks posed by the use of chemical agents.

When using chemicals it is important to have accurate information on their properties, so as to be able to identify possible dangers and determine the most appropriate means for their handling.

Internationally established norms and regulations exist on the need to specify the characteristics of a chemical substance on its label.

**Classification of chemical compounds**

The physico-chemical properties and toxicity of chemical substances in terms of the danger they represent can be classified accordingly:

- toxic and very toxic;
- corrosive;
- irritant;
- inflammable and extremely inflammable;
- combustible;
- noxious.

Chemical substances that cause cellular changes in an organism can be grouped into:

- *Mutagen*: Compounds or substances that produce chemical changes in the composition of the bases of DNA, such as 5-bromouracil, 2-aminopurine, nitric acids and mustard gases.
- *Carcinogen*: Chemical agents whose adverse effects are promotion of tumours in animals and humans. Many of the substances that cause mutations are also carcinogens. Among those used in laboratories are xylol, benzine, benzedine, tar, phenols and sulphur.
- *Teratogen*: Chemicals that produce birth defects following malformation of the foetus.
- *Other:* Among those substances deemed to have a chemical risk there are some that do not represent a high risk, but others that can provoke violent reactions and explode or become extremely toxic. These are termed incompatible chemical compounds and they must be stored and handled with care.

The handling of solvents and gases, as well as ordinary chemicals, is potentially dangerous, but is easily managed with adequate preparation and knowledge. Potential problems arising from mismanagement include electrostatic combustion of organic solvents and the danger of explosion from inflammable gases and peroxides. Many of the chemical substances in current use in facilities can cause dangerous

reactions, such as fires, and have to be stored carefully with full understanding of their properties.

Safety principles and risks associated with chemical substances are summarized in Box B.1:

BOX B.1

## SAFETY PRINCIPLES FOR HANDLING CHEMICAL SUBSTANCES

**Principles of safety for chemical substances**

- Read the labels and other sources of information.
- Pay attention when handling.
- Mind your personal safety by using recommended means of protection.
- Transport the substances in secure containers.
- Do not taste or smell chemicals.
- Minimize vapour production by not leaving containers open.
- Store in ventilated places according to manufacturers' instructions.
- Use ventilated fume cupboards to capture toxic emissions.
- Do not smoke, eat or keep food in laboratories.
- Do not pipette by mouth.
- Recognize symptoms of exposure.
- Inform about all accidents and incidents.
- Do not work wearing contact lenses.
- Know the emergency procedures.
- Know where the emergency equipment is.

**Risks linked with chemical substances**

- Illnesses and changes in health.
- Fires and explosions.
- Poisoning.
- Contamination of the environment.

**General precautions for handling chemical substances**

- Use gloves and protective glasses.

- Work in a flow chamber.
- Avoid contact with skin, eyes and mucous membranes.
- Clean splashes immediately with lots of water.
- Do not smoke, eat or drink in laboratories.
- Take note of the symbols for level of danger.

The form (liquid, solid, gaseous) of the chemical substance greatly influences its effect. Short exposure to high concentrations of a substance can result in acute effects, while prolonged exposure to lower concentrations can result in chronic effects, manifested as biological changes that disturb normal functions and impair health and the capacity to work.

A summary of facility design and storage and handling of chemical substances is provided in Box B.2:

BOX B.2

## FACILITY DESIGN FOR WORK WITH CHEMICAL SUBSTANCES

**General methods the facilities should put in place**

- Place two doors in opposition.
- Protect the networks for gas and electricity.
- Ventilation should be sufficient to avoid build-up of vapour, install supplementary ventilation for emergency cases.
- Install emergency high-pressure showers to cope with emergencies.
- Place sinks near to working areas.
- Install an auxiliary storeroom in a well-ventilated place to avoid storage near the areas of work.
- Make sure there are emergency procedures in place.

**Storing chemical substances**

- Keep inflammable and non-inflammable products separate.
- Maintain products in groups

according to danger posed, corrosives, toxic oxidants etc., making sure that incompatible substances are not brought together.
- Keep substances in their original containers.
- Keep sunlight out.
- Keep heavy containers on the bottom shelves.
- Keep the most reactive substances at the lowest levels.
- Oxidizing agents (ethyl ether, isopropyl ether), once opened, must not be stored for more than six months.
- Carcinogens, inflammables and active poisons require special storage.

## B.2 Physical risks

**PHYSICAL RISKS**
All risks related to physical factors and forces, e.g. mechanical, thermal, electrical, radiation and fire.

Physical risks, posing a considerable danger to personnel, are to be found in all areas of a facility and accidents can be different in nature:

- *Mechanical*: Mechanical accidents most often occur when storerooms are inadequately cleaned, there is inadequate illumination, movement is obstructed and objects are badly located. Motors, centrifuges, compressors and other objects with potential energy, such as gas cylinders etc., represent equipment that needs to be handled with specific attention.
- *Thermal*: Among others, high temperatures can cause burns (ovens, autoclaves) and low temperatures can cause hypothermia (cold rooms, liquid nitrogen).
- *Electrical*: Includes the possibility of shock, fire and the source of ignition for particular reactive chemicals in the laboratory (inflammable vapours and gases). Among the causes are faulty electric cables, bad connections and overloading. In facilities with ovens, incubators, autoclaves etc., there is the risk of electrical discharge and severe burns when handling is incorrect or when precautions are not taken and protective equipment is not used. Such accidents are rare but when they occur can be fatal.

- *Radiation*: Ionizing radiation (alpha, beta, gamma, X-rays, neutrons) is potentially the most serious risk and its sources are radioactive isotopes, X-ray equipment and electron microscopes. Other sources of non-ionizing radiation can be important, such as UV light and lasers. Consequences of exposure to high levels of radiation can be burns to the skin, cancer, alterations to the blood system, reduction in bone marrow, cataracts, immunological defects and death.
- *Fire*: Caused by various sources of heat, faulty electrical equipment, defective electrical wires, incorrect positioning of equipment and handling of inflammable and explosive materials.

It is important that refrigerators are of the domestic type, they should be explosion-proof and it is important that the wiring of the thermostat is outside the refrigerator.

According to WHO, the most common causes of fire in facilities are:

- electrical overload; installing new equipment without considering the consequences of adding equipment to the circuit;
- poor maintenance of the electrical system;
- gas pipes and electric cables that are too long;
- equipment that is plugged in when not necessary;
- naked flames;
- poor handling of phosphorus;
- lack of care in handling inflammable materials;
- explosive and inflammable chemicals stored in regular refrigerators.

Equipment for fighting fires should be situated near to the doors of the facility, in strategic areas in corridors and rooms and should include hoses, buckets and fire extinguishers (including water, carbon dioxide, carbonated ice, foam and bromochlorodifluoromethane (Halon 1211, BCF) extinguishers). Equipment should be regularly maintained and checked.

It is very important to install smoke detectors and alarms as part of a detection system that allows rapid response.

In Table B.2 common types of fire and control methods are given:

Table B.2 | **How to extinguish fires**

| Type | Combustible material | Extinguisher | | | | |
|---|---|---|---|---|---|---|
| | | Water | Foam | $CO_2$ | Chemical dusts | Special agents |
| A | Wood, textiles, paper and solids in general | Yes | Yes | Yes[1] | Yes | No |
| B | Inflammable liquids or solids with low combustion points (petrol, acetone, grease etc.) | No[2] | Yes | Yes | Yes | Yes[1] |
| C | Electrical equipment | No[3] | No[3] | Yes | Yes | Yes[1] |
| D | Metals and combustible materials | No[4] | No[4] | No[4] | Yes[1] | Yes |

[1] Can be used but less effective
[2] Incompatible with water, with which it can cause fire
[3] Electrical conductor
[4] Violent reactions with water, generating hydrogen and producing explosive mixtures with air

## B.3 Psycho-physiological and environmental conditions

An additional risk group is composed of human and environmental factors that can considerably increase the risk associated with other factors. The risks are related to aptitudes and capacities to carry out the work, physical and psychological state of the staff, intellectual capacity, training, working atmosphere and conditions. A large proportion of the problems that can arise during a process with a particular attached risk originate from human error.

Such influencing factors can be:

- physiological state;
- psychological state;
- intellectual capacity and job training;
- conduct;
- psycho-social stress.

Environmental conditions have to be taken into account when carrying out tasks in a range of facilities, including temperature, humidity, ventilation and illumination.

A large percentage of problems that can arise in a process with a determined risk originate from human error, and depend on the level of training, such as in the use of safety equipment. Errors and accidents caused by untrained personnel can ultimately result in serious consequences for personnel and the environment in terms of health damage, pollution and economic losses.

ANNEX 2

# PRINCIPLES AND METHODOLOGIES FOR THE ENVIRONMENTAL RISK ASSESSMENT

The following information regarding the establishment of an environmental risk assessment was extracted from legislation of the European Community (EC, 2001). Further guidance literature providing detailed explanations concerning the individual steps of the ERA has been prepared and is available online (EFSA, 2006a,b). Further, the requirements for information that must be submitted when handing in an application for a GMO release prove useful in determining the individual points that must be investigated in the ERA (see EC, 2001, Annex III). Connor *et al*. (2003) have also provided an interesting paper, critically investigating the ERA procedure and general risk perception and discussing major areas of environmental concerns associated with GM crops. The information provided here might serve as guidelines for the establishment of individual country environmental risk assessment procedures and relevant legislation.

## A OBJECTIVE

The objective of an ERA is, on a case by case basis, to identify and evaluate potential adverse effects of the GMO, either direct or indirect, immediate or delayed, on human health and the environment which the deliberate release or

the placing on the market of GMOs may have. The ERA should be conducted with a view to identifying if there is a need for risk management and, if so, the most appropriate methods to be used.

## B GENERAL PRINCIPLES

In accordance with the precautionary principle, the following general principles should be followed when performing the ERA:

- Identified characteristics of the GMO and its use which have the potential to cause adverse effects should be compared to those presented by the non-modified organism from which it is derived and its use under corresponding situations;
- The ERA should be carried out in a scientifically sound and transparent manner based on available scientific and technical data;
- The ERA should be carried out on a case by case basis, meaning that the required information may vary depending on the type of the GMOs concerned, their intended use and the potential receiving environment, taking into account, i.a., GMOs already in the environment;
- If new information on the GMO and its effects on human health or the environment becomes available, the ERA may need to be readdressed in order to: (I) determine whether the risk has changed; (II) determine whether there is a need for amending the risk management accordingly.

## C METHODOLOGY

### C.1 Characteristics of GMOs and releases

Depending on the case, the ERA has to take into account the relevant technical and scientific details regarding characteristics of:

- The recipient or parental organism(s);
- The genetic modification(s), be it 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.

Information from releases of similar organisms and organisms with similar traits and their interaction with similar environments can assist the ERA.

## C.2 Steps in the ERA

In drawing conclusions for the ERA the following points should be addressed:

**1. Identification of characteristics which may cause adverse effects:**
Any characteristics of the GMOs linked to the genetic modification that may result in adverse effects on human health or the environment should be identified. A comparison of the characteristics of the GMO(s) with those of the non-modified organism under corresponding conditions of the release or use will assist in identifying the particular potential adverse effects arising from the genetic modification. It is important not to discount any potential adverse effect on the basis that it is unlikely to occur. Potential adverse effects of GMOs will vary from case to case, and may include:

- Disease to humans including allergenic or toxic effects;
- Disease to animals and plants including toxic, and in some case, allergenic effects;
- Effects on the dynamics of populations of species in the receiving environment and the genetic diversity of each of these populations;
- Altered susceptibility to pathogens facilitating the dissemination of infectious diseases and/or creating new reservoirs or vectors;
- Compromising prophylactic or therapeutic medical, veterinary, or plant protection treatments, for example by transfer of genes conferring resistance to antibiotics used in human or veterinary medicine;

» Effects on biogeochemistry (biogeochemical cycles), particularly carbon and nitrogen recycling through changes in soil decomposition of organic material.

Adverse effects may occur directly or indirectly through mechanisms which may include:

» The spread of the GMO(s) in the environment,
» The transfer of the inserted genetic material to other organisms, or the same organism whether genetically modified or not,
» Phenotypic and genetic instability,
» Interactions with other organisms,
» Changes in management, including, where applicable, in agricultural practices.

**2. Evaluation of the potential consequences of each adverse effect, if it occurs**

The magnitude of the consequences of each potential adverse effect should be evaluated. This evaluation should assume that such an adverse effect will occur. The magnitude of the consequences is likely to be influenced by the environment into which the GMO(s) is (are) intended to be released and the manner of the release.

**3. Evaluation of the likelihood of the occurrence of each identified potential adverse effect**

Major factors in evaluating the likelihood or probability of adverse effects occurring are the characteristics of the environment into which the GMO(s) is intended to be released, and the manner of the release.

**4. Estimation of the risk posed by each identified characteristic of the GMO(s)**

An estimation should be made as far as possible of the risk to human health or to the environment posed by each characteristic of the GMO identified as having the potential to cause adverse effects. This can be done by combining the likelihood of the adverse effect occurring with the magnitude of the consequences of any such occurrence.

**5. Application of management strategies for risks from the deliberate release or marketing of GMO(s)**

The risk assessment may identify risks that require management and how best to manage them, and a risk management strategy should be defined.

**6. Determination of the overall risk of the GMO(s)**

An evaluation of the overall risk of the GMO(s) should be made taking into account any risk management strategies which are proposed.

## D CONCLUSIONS ON THE POTENTIAL ENVIRONMENTAL IMPACT FROM THE RELEASE OR THE PLACING ON THE MARKET OF GMOs

On the basis of an ERA carried out in accordance with the principles and methodology outlined in sections B and C, information on the points listed in sections D1 or D2 should be included, as appropriate, in notifications with a view to assisting in drawing conclusions on the potential environmental impact from the release or the placing on the market of GMOs:

### D.1 In the case of GMOs other than higher plants

1. Likelihood of the GMO to become persistent and invasive in natural habitats under the conditions of the proposed release(s).
2. Any selective advantage or disadvantage conferred to the GMO and the likelihood of this becoming realized under the conditions of the proposed release(s).
3. Potential for gene transfer to other species under conditions of the proposed release of the GMO and any selective advantage or disadvantage conferred to those species.
4. Potential immediate and/or delayed environmental impact of the direct and indirect interactions between the GMO and target organisms (if applicable).

5. Potential immediate and/or delayed environmental impact of the direct and indirect interactions between the GMO with non-target organisms, including impact on population levels of competitors, prey, hosts, symbionts, predators, parasites and pathogens.
6. Possible immediate and/or delayed effects on human health resulting from potential direct and indirect interactions of the GMO and persons working with, coming into contact with or in the vicinity of the GMO release(s).
7. Possible immediate and/or delayed effects on animal health and consequences for the feed/food chain resulting from consumption of the GMO and any product derived from it, if it is intended to be used as animal feed.
8. Possible immediate and/or delayed effects on biogeochemical processes resulting from potential direct and indirect interactions of the GMO and target and non-target organisms in the vicinity of the GMO release(s).
9. Possible immediate and/or delayed, direct and indirect environmental impacts of the specific techniques used for the management of the GMO where these are different from those used for non-GMOs.

## D.2 In the case of genetically modified higher plants:

1. Likelihood of the GMHP becoming more persistent than the recipient or parental plants in agricultural habitats or more invasive in natural habitats.
2. Any selective advantage or disadvantage conferred to the GMHP.
3. Potential for gene transfer to the same or other sexually compatible plant species under conditions of planting the GMHP and any selective advantage or disadvantage conferred to those plant species.
4. Potential immediate and/or delayed environmental impact resulting from direct and indirect interactions between the GMHP and target organisms, such as predators, parasitoids, and pathogens (if applicable).
5. Possible immediate and/or delayed environmental impact resulting from direct and indirect interactions of the GMHP with non-target organisms (also taking

into account organisms which interact with target organisms), including impact on population levels of competitors, herbivores, symbionts (where applicable), parasites and pathogens.

6. Possible immediate and/or delayed effects on human health resulting from potential direct and indirect interactions of the GMHP and persons working with, coming into contact with or in the vicinity of the GMHP release(s).
7. Possible immediate and/or delayed effects on animal health and consequences for the feed/food chain resulting from consumption of the GMO and any products derived from it, if it is intended to be used as animal feed.
8. Possible immediate and/or delayed effects on biogeochemical processes resulting from potential direct and indirect interactions of the GMO and target and non-target organisms in the vicinity of the GMO release(s).
9. Possible immediate and/or delayed, direct and indirect environmental impacts of the specific cultivation, management and harvesting techniques used for the GMHP where these are different from those used for non-GMHPs.

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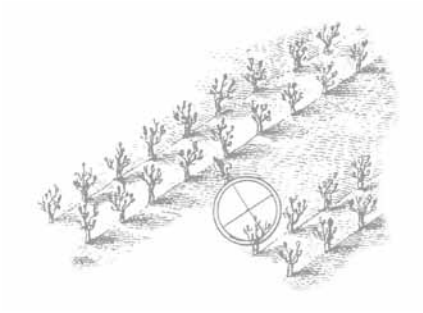

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# Biosafety Resource Book

**MODULE C**

**RISK ANALYSIS**

provides basic information on biological risks, concepts, principles, and methodologies of risk assessment, risk management and risk communication. It focuses on crop biotechnology and environmental risk assessment of GM crops since these are of immediate interest to most countries.

For additional information please consult
**www.fao.org/biotech**
or contact
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