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AD HOC TECHNICAL EXPERT GROUP ON RISK ASSESSMENT AND RISK MANAGEMENT UNDER THE CARTAGENA PROTOCOL ON BIOSAFETY
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Item 3.2 of the provisional agenda*

ALIGNMENT OF THE CONTENTS OF THE "ROADMAP FOR RISK ASSESSMENT OF LIVING MODIFIED ORGANISMS" AND "TRAINING MANUAL ON RISK ASSESSMENT OF LIVING MODIFIED ORGANISMS"

1. In its decision BS-VI/12, the Conference of the Parties serving as the meeting of the Parties to the Protocol (COP-MOP) mandated the Online Forum on Risk Assessment and Risk Management and the Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management to "[c]oordinate, in collaboration with the Secretariat, the development of a package that aligns the Guidance on Risk Assessment of Living Modified Organisms (e.g. the Roadmap) with the training manual 'Risk Assessment of Living Modified Organisms' in a coherent and complementary manner, for further consideration of the Parties, with the clear understanding that the Guidance is still being tested".

2. The present document was prepared by the Secretariat on the basis of discussions held under the Online Forum and the AHTEG[1] to serve as a working document during the face-to-face meeting of the AHTEG to be held in Bonn, Germany from 2 to 6 June 2014. It contains an alignment of the contents of the "Roadmap for Risk Assessment of Living Modified Organisms" and the contents of the "Manual for Risk Assessment of Living Modified Organisms".

* UNEP/CBD/BS/AHTEG-RA&RM/5/1.
[1] Available at http://bch.cbd.int/onlineconferences/forum_ra/discussion.shtml.

Module 1:

Overview of Biosafety and the Cartagena Protocol on Biosafety

Introduction to biosafety
and the
Cartagena Protocol on Biosafety

History of the Protocol

The United Nations Conference on Environment and Development (also known as the "Earth Summit"), held in Rio de Janeiro in 1992 marks a significant achievement in the overall policy of the United Nations on the environment. Several documents resulting from that meeting constitute the basis of the international law on biosafety, such as Agenda 21, the Rio Declaration on Environment and Development and the United Nations Convention on Biological Diversity.

Agenda 21 is a comprehensive programme for action in social and economic areas and for conserving and managing the natural resources. Its chapter 16 addresses the "Environmentally sound management of biotechnology" (see [information icon]) by recognising that modern biotechnology can make a significant contribution to enhancing food security, health and environmental protection, and outlining the need for international agreement on principles to be applied to risk assessment and management and set out the implementation of safety mechanisms on regional, national, and international levels.

The Rio Declaration on Environment and Development is a series of principles defining the rights and responsibilities of States. Principle 15 allows countries to take precautionary action to prevent environmental degradation where there are threats, but no conclusive evidence, of serious or irreversible damage (see [information icon]).

[information icon]: Agenda 21, chapter 16, paragraph 29

[information icon]: Principle 15 of the Rio Declaration on Environment and Development

History of the Protocol

The Convention on Biological Diversity (CBD) was inspired by the global community's growing commitment to sustainable development. It represents a dramatic step forward in the conservation of biological diversity, the sustainable use of its components, and the fair and equitable sharing of benefits arising from the use of genetic resources. The CBD addresses access to biotechnology and the sharing of its benefits in articles 16 ("Access to and Transfer of Technology") and 19 ("Handling of Biotechnology and Distribution of its Benefits"). The issue of safety in biotechnology is addressed in articles 8(g) and 19(3) of the CBD.

More specifically, in Article 8(g) [information icon], Parties to the CBD are called upon to establish or maintain means to regulate, manage or control the risks associated with the use and release of living modified organisms (LMOs) resulting from biotechnology which are likely to have adverse impacts on the conservation and sustainable use of biological diversity. In Article 19(3) [information icon], the Parties are called upon to consider the need for and modalities of a protocol for the safe transfer, handling and use of LMOs resulting from biotechnology that may have adverse effect on the conservation and sustainable use of biological diversity.

[information icon]: Article 8(g). In-situ Conservation of the Convention on Biological Diversity

[information icon]: Article 19(3). Handling of Biotechnology and Distribution of its Benefits of the Convention on Biological Diversity

History of the Protocol

Taking into account the provisions above, the Conference of the Parties to the Convention on Biological Diversity decided, at its second meeting, to develop a protocol on biosafety, specifically focusing on the transboundary movement of LMOs that may have adverse effects on the conservation and sustainable use of biological diversity taking into account human health.

As a preliminary tool to serve as interim guidance for biosafety, a set of International Technical Guidelines for Safety in Biotechnology was drafted by UNEP and adopted by the Global Consultation of Government-designated Experts in Cairo, Egypt in December 1995.

In 1996, the Conference of the Parties for the Convention on Biological Diversity established an Open-ended Ad Hoc Working Group on Biosafety to develop a draft protocol. This Working Group met six times between 1996 and 1999 and, at the conclusion of its last meeting, a draft protocol was submitted for consideration by the Conference of the Parties at an extraordinary meeting in February 1999, in Cartagena, Colombia. The Conference of the Parties was not able to finalize its work in Cartagena. As a result, the Conference of the Parties suspended its first extraordinary meeting and agreed to reconvene as soon as possible.

The Conference of the Parties reconvened and adopted the Cartagena Protocol on Biosafety on 29 January 2000 in Montreal, Canada. The Protocol entered into force on 11 September 2003 upon ratification by the fiftieth Party. As of September 2011, 161 Parties had acceded/ratified the Protocol.

What is Biosafety?	
In its broad sense, the term biosafety refers to the protection of human health and the environment from potential harm due to biological agents. Under the Convention on Biological Diversity (CBD), and more specifically under the Cartagena Protocol on Biosafety ("the Protocol"), the term biosafety essentially refers to safety procedures aimed at regulating, managing or controlling the risks associated with the use and release of LMOs resulting from biotechnology which are likely to have adverse environmental impacts that could affect the conservation and sustainable use of biological diversity, taking also into account risks to human health. Biosafety comprises multidisciplinary scientific fields including, but not limited to biology, ecology, microbiology, molecular biology, animal and plant pathology, entomology, agriculture and medicine as well as legal and socio-economic considerations, and public awareness. The text of the Cartagena Protocol on Biosafety is available at http://bch.cbd.int/protocol/text.	

What are living modified organisms?

The definition of "Living modified organism" (LMO) is spelled out in article 3, paragraph (g) of the Protocol [information icon] .

According to the Protocol, an LMO is an organism that contains a novel combination of genetic material and results from (i) in vitro modification of nucleic acid (DNA or RNA) molecules; or (ii) cell fusion between organisms of different taxonomic families. In either case, for an organism to be considered an LMO, the techniques used in its development should be ones "that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection".

Modern biotechnology techniques include, but are not limited to, in vitro DNA and RNA techniques for the modification of genetic material (e.g. by insertion, modification or deletion of genes or other nucleic acid sequences) in all types of organisms, such as plants, animals, microbes and viruses.

[information icon]: Article 3. "Living modified organism" and "modern biotechnology"

Objective and scope of the Protocol	
The objective of the Protocol is "to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on transboundary movements". The Protocol establishes rules and procedures for the safe handling, transfer, and use of LMOs. The Protocol focuses on the transboundary movement of LMOs destined for introduction into the environment and those intended for use directly as food, feed or for processing. The protocol seeks to protect biological diversity, taking into account human health, from the potential risks posed by living modified organisms resulting from modern biotechnology (UNEP, 2006). All LMOs that may have adverse effects to biodiversity or human health are within the scope of the Protocol. Nevertheless, some types of LMOs may be excluded from some provisions, as indicated below: [information icon] ***[information icon]: Scope of the Cartagena Protocol on Biosafety***	

Living modified organisms for intentional introduction into the environment – Advanced Informed Agreement (AIA)	
The Advanced Informed Agreement (AIA) defines mandatory procedures to be applied to the first transboundary movement of an LMO for intentional introduction into the environment. LMOs intended for direct use as food, feed, or for processing are subject to a different procedure, as outlined in the next section. The AIA procedure begins with the Party of export or the exporter notifying the Party of import of the proposed transboundary movement of an LMO for intentional introduction into the environment. The notification must contain at a minimum the information specified in Annex I of the Protocol including, among other things, contact details of the exporter and importer, name and identity of the LMO and its intended use, as well as a risk assessment report consistent with Annex III of the Protocol. The Party of import has 90 days to acknowledge the receipt of the notification, and 270 days to communicate its decision to the notifier and the Biosafety Clearing-House (BCH). In its decision, the Party of import may approve or prohibit the import of the LMO, request further information or extend the decision period for a defined amount of time. If the Party of import does not communicate its decision within 270 days, it should not be understood that consent was given (unless article 10, paragraph 2(b) applies). A decision that approves the use of an LMO may be done with or without conditions. If there are conditions, the decision must set out the reasons for the conditions. ***[information icon]: Application of the Advanced Informed Agreement (AIA) procedure***	

Living modified organisms for direct use as food, feed, or for processing (LMO-FFPs)	
According to Article 11 of the Protocol, a Party that makes a final decision regarding domestic use, including placing on the market, of an LMO that may be subject to transboundary movement for direct use as food or feed, or for processing shall submit to the BCH the information specified in Annex II of the Protocol, within fifteen days. This information includes, among other things, the name and identity of the LMO and its approved uses, as well as a risk assessment report consistent with Annex III of the Protocol (see Article 11(1)).	
Competent National Authorities	
Each Party should designate one or more competent national authorities (CNAs) who will perform the administrative functions required by the Protocol and are authorized to take decisions on the LMOs for which they are designated (see Module 2).	

Risk Assessment (Article 15 and Annex III)

Article 15 of the Protocol sets out the provisions for Parties to conduct risk assessments of LMOs. It requires that risk assessments be carried out in a scientifically sound manner in accordance to Annex III and taking into account recognized risk assessment techniques.

While the Party considering permitting the import of an LMO is responsible for ensuring that a risk assessment is carried out, it has the right to require the exporter to do the work or to bear its cost. This is particularly important for many developing countries (SCBD, 2003).

The Protocol, therefore, empowers governments to decide whether or not to accept imports of LMOs on the basis of risk assessments. These assessments aim to identify and evaluate the potential adverse effects that an LMO may have on the conservation and sustainable use of biodiversity in the receiving environments.

Annex III sets out the general principles and methodology for the risk assessment process. Annex III also contains a number of steps for conducting the risk assessment as well as points to consider on the technical and scientific details regarding, for example, the characteristics of the genetic modification, biological characteristics of the LMO, differences between the LMO and its recipient organism, its intended use, the likely receiving environment, amongst other things.

The general principles for conducting a risk assessment under the Protocol are that (i) it must be carried out in a scientifically sound and transparent manner and on a case-by-case basis, (ii) lack of scientific knowledge or scientific consensus should not necessarily be interpreted as indicating a particular level of risk, an absence of risk, or an acceptable risk, and (iii) risks of LMOs should be considered in the context of the risks posed by the non-modified recipients or parental organisms in the likely potential receiving environment.

Individual Parties use these general principles to guide the development and implementation of their own national risk assessment process (see Module 2). The following slides contain considerations regarding some of the general principles for risk assessment.

Risk Assessment (Article 15 and Annex III)	
Scientific soundness – The Cartagena Protocol explicitly states that risk assessments should be carried out in a scientifically sound manner. The principle of scientific soundness entails that risk assessments are to be undertaken in a systematic way on the basis of verifiable and reproducible information by, for example, reporting on methods and data in sufficient detail to enable others to repeat the steps of the risk assessment independently. Some countries have integrated this principle into their own procedures with specific suggestions about what type of information is appropriate for use in a risk assessment. In many cases, different sources and criteria for scientifically sound information have been set, ranging from scientific literature, studies presented by the notifier and expert opinions, etc. Consultations among scientific experts may also be considered as an appropriate means for gathering such information. **Transparency** – Annex III states that risk assessments should be conducted in a transparent manner. Most countries with National Biosafety Frameworks (NBFs) have procedures in place to ensure the transparency of risk assessments. The CNAs often show what transparency mechanism is in place to handle notifications and how the mechanism is applied in each case. The level of transparency, however, may range from public notification to broad public involvement. Some countries, for instance, make the necessary requirements for conducting risk assessments available online and, if an approval is granted for release of an LMO into the environment, a public notification is usually issued by posting the release online (see also provisions of Article 23 on "Public Participation" and the section below on "Stakeholder participation"). ***EXAMPLE: The case-by-case basis is fundamental to risk assessment of LMOs*** ***EXAMPLE: Need for transparency***	

The Biosafety Clearing-House and other provisions

The Biosafety Clearing-House (BCH) is a mechanism set up under the Protocol to facilitate the exchange of information on LMOs and assist countries that are Parties to the Protocol to better comply with their obligations.

The BCH provides open and easy access to a variety of scientific, technical, environmental, legal and capacity building information provided in all 6 languages of the UN.

The BCH contains the information that must be provided by Parties to the Protocol, such as decisions on release or import of LMOs, risk assessments, competent national authorities, and national laws.

Governments that are not Parties to the Protocol are also encouraged to contribute information to the BCH, and in fact a large number of the decisions regarding LMOs have been registered in the BCH by non-Party governments.

The records of decisions, risk assessments, LMOs, donor and recipient organisms, and DNA sequences are cross-referenced in a way that facilitates data retrieval. For instance, while looking at an LMO record, all the records for the risk assessment that reference that specific LMO can be easily accessed and retrieved.

The BCH also contains other relevant information and resources, including information on national contacts, capacity-building, a roster of government-nominated biosafety experts, and links to other websites, publications and databases through the Biosafety Information Resource Centre (BIRC).

Other provisions under the Protocol

In addition to the provisions above, the Protocol also requires the Parties to the Protocol, consistent with their international obligations, to consult the public during the decision-making process regarding LMOs (Article 23); make the results of such decisions available to the public (Article 23) and allow the decision-making process to take into account socio-economic considerations arising from the impact of the LMOs on the conservation and sustainable use of biodiversity (Article 26).

Module 2:

Preparatory Work – Understanding the context in which a risk assessment will be carried out

Introduction	
Prior to receiving an LMO notification, risk assessors[(1)] may need to familiarise themselves with issues such as environmental protection goals, regulatory requirements and compliance of a national framework with the Protocol to gain an understanding of the general framework within which the risk assessment must be carried out to comply with international obligations, national laws and administrative procedures. The biosafety framework of each country may address administrative matters by establishing mechanisms for (i) the selection of risk assessors and/or establishment of advisory bodies; (ii) handling confidential information (Article 21); (iii) public awareness and participation (Article 23); and (iv) if and how socio-economic considerations should be taken into account in the decision-making process (Article 26), amongst other things. The following sections of this module provide an overview on how some issues might be considered by risk assessors prior to undertaking a risk assessment.	

National context

National protection goals	
Countries are sovereign in setting their own goals such as the protection of the environment, biodiversity or the health of their citizens. In so doing, they often adopt environmental and public health strategies as part of their national policy and legislation. These strategies, in turn, are often derived from, or compliant with, broader internationally agreed instruments. Environmental and health policies and laws often define sets of "protection goals", which are defined and valued environmental outcomes that guide the formulation of strategies for the management of activities that may affect the environment. Some protection goals are defined broadly (e.g. conservation of biodiversity) while others are more specific (e.g. protection of a threatened or endangered species). The context for all (environmental) risk assessments is set by the relevant protection goals, regardless of whether they are broad or specific. ***EXAMPLE: Protection goals – The Aichi Biodiversity Targets*** ***EXAMPLE: Biodiversity protection goal in the European Union***	

Assessment endpoints

In addition to the protection goals, national legislations sometimes also define "assessment endpoints". An assessment endpoint is an explicit expression of the environmental value that is to be protected, operationally defined as an entity (such as salmon or honeybees, soil quality) and its attributes (such as their abundance, distribution or mortality).

Ecological assessment endpoints, for instance, are most easily expressed in terms of impacts on a valued species (e.g. survival and reproduction of the yellow fin tuna). Any component, from virtually any level of biological organization or structural form that is recognized as an entity that needs to be protected, can be considered an assessment endpoint.

Once a risk assessment has been triggered, the risk assessor(s) will need to identify the relevant protection goals and assessment endpoints when these are available. The risk assessor(s) then determines which assessment endpoints are meaningful to the specific case at hand to ensure that the protection goals will be adequately covered. For example, the regulatory framework of a country may identify "agricultural biodiversity" as one of its protection goals and the risk assessor(s) may be asked to consider, as an assessment endpoint, the abundance of a valued species, for example an insect pollinator, in the environment where the LMO may be released.

Selecting endpoints is among the most critical aspects when preparing a conceptual model for the risk assessment as it contributes to setting the stage for the risk assessment and the remaining steps of the processIn conclusion, before undertaking a risk assessment of an LMO, risk assessors and other biosafety officers should understand national protection goals and the importance of deciding upon relevant assessment endpoints in order to plan a risk assessment. Issues related to protection goals and relevant assessment endpoints are outlined in more detail in Module 3 under "Planning phase".

EXAMPLE: Assessment endpoint

National Biosafety Framework

Many countries address biosafety related issues through a large process that includes the development and implementation of a National Biosafety Framework (NBF). An NBF consists of a combination of policy, legal, administrative and technical instruments that are set in place to address the safety of the environment and human health in relation to modern biotechnology.

In most cases, the administration of biosafety responsibilities is either shared by several government departments (e.g. environment, agriculture, health, science) or centralized and managed by one office which is responsible for the coordination of biosafety issues over a number of government departments.

The choice of framework most often reflects existing regulatory structures and the resources available at the national level for implementing the biosafety regulations.

There has been a significant increase in the number of countries that possess NBFs. A global initiative funded by the Global Environment Facility (GEF) and its implementing agencies helped this process by providing administrative and technical assistance to countries for developing and implementing their NBFs in accordance with their obligations under the Cartagena Protocol.

Countries' requirements and priorities resulted in the development of national biosafety policies in a variety of forms. Some choose to develop a stand-alone policy on biosafety, whilst others formulated combined policies on biotechnology and biosafety. Some policies are part of wider policies on biodiversity conservation and environmental protection, trade related issues, biosecurity and quarantine, or established within the overall context of sustainable development or Agenda 21 (UNCED, 1992).

As of May 2012, through the GEF funded initiatives, 121 developing countries have completed the development phase of their National Biosafety Frameworks and made them available online.

Competent National Authorities

While the NBFs consist of policy, legal, administrative and technical instruments, the institutional responsibility for decision-making and for risk assessments of LMOs usually falls to the Competent National Authorities (CNAs). According to the Cartagena Protocol, each Party is to designate one or more CNAs to perform the administrative functions required by the Protocol.

Additionally, according to the Protocol, Parties are obliged to clearly indicate, though the Biosafety Clearing-House (BCH), any existing laws, regulations or guidelines for implementation of the Protocol, as well as the names and addresses of its CNA(s).[(3)]

The NBFs usually set out competencies and procedures depending on the LMO (e.g. the type of LMO or its intended use). As such, risk assessments may be assigned to different CNAs within the same country.

The options chosen by countries for the institutional setup of CNAs in each NBF include (i) a single CNA receiving and processing all requests regarding LMOs, or (ii) more than one CNA, each with different responsibilities and with either a single or multiple routes for the submission of applications regarding LMOs.

In cases when a Party designates more than one CNA, information on their respective responsibilities should be clearly stated and made available to the BCH. This information may include, for instance, which CNA is responsible for which type of LMO.

In most of the draft NBFs, developed by countries assisted by the UN Environment Programme (UNEP) as a GEF implementing agency, the responsibility of risk assessment has been assigned to the CNA(s) or the overall biosafety body, with or without advice from either an ad hoc scientific advisory body, or an established advisory committee.

EXAMPLE: Competent National Authorities in Mexico

Competent National Authorities

National Biosafety Frameworks, when established, define the conditions that trigger the need for a risk assessment. Without prejudice to any right of a country to subject all living modified organisms to a risk assessment, under the Cartagena Protocol two specific cases require mandatory risk assessments prior to making a decision: a) the first intentional transboundary movement of a living modified organism for intentional introduction into the environment of the Party of import, and b) a final decision regarding the domestic use of a living modified organism, including its placement on the market, that may be subject to transboundary movement for direct use as food or feed, or for processing.

Upon receiving a request that triggers a risk assessment, the CNA takes several actions as part of a process to ensure that a scientifically sound risk assessment is carried out by risk assessors. These may include the following:

(a) Reviewing the LMO notification for completeness against a pre-determined list of information;

(b) Specifying the terms of reference of the risk assessment and the information expected in the final report;

(c) Identifying one or more risk assessors who will conduct and manage the risk assessment.

In case of a notification for transboundary movement to countries that are Parties to the Cartagena Protocol this list shall contain at a minimum the information specified in Annex I (in case of an application for the intentional introduction into the environment) or in Annex II (in case of a decision regarding LMOs intended for direct use as food or feed, or for processing).

EXAMPLE: Competent National Authority(ies) and National Biosafety Frameworks

EXAMPLE: Institutional responsibilities for risk assessment

Practices and principles	
The risk assessment process includes practices and principles that may differ between countries. As seen in Module 1, Annex III of the Protocol lists the general principles for risk assessment. Individual Parties use these general principles to guide the development and implementation of their own national risk assessment process. As such, the general principles for risk assessment may be incorporated into the country's laws, or be included in guidelines adopted by the country. ***EXAMPLE: Risk assessment practices in various countries***	
Other national and international obligations	
A country may have national laws and international obligations, such as trade agreements, that are not directly related to biosafety or to the environment but may influence how the risk assessor(s) will proceed once a risk assessment of an LMO is triggered. Such obligations may, for instance, affect establishing the scope of the risk assessment (see Module 3). For examples of relevant international treaties and agreements see Module 1.	

Expert advice and the role of the risk assessor(s)

Scientific advisory body	
In some countries the necessary expertise required to carry out risk assessments of LMOs resides in the regulatory agencies and the risk assessments are carried out internally. In such cases, these agencies typically have the option of requesting additional expert input if deemed necessary. On the other hand, the regulatory frameworks of many other countries call for the establishment of scientific expert panels on an ad hoc basis once a risk assessment has been triggered. In such cases, a CNA assesses what expertise is needed for each specific case and pools together an external team of risk assessors consisting of experts in the relevant scientific fields. Such an advisory body may contain a pool of experts at the national, regional or international levels, who can be called upon to assist the mandated risk assessor(s) when a need arises. A scientific advisory body allows the CNA to quickly engage the appropriate expertise for a particular risk assessment. In cases when a CNA establishes a team or panel of risk assessors, it typically designates one of the risk assessors to coordinate the risk assessment process. ***EXAMPLE: How scientists are involved in the risk assessment process***	

Responsibilities of the risk assessor(s)

National frameworks establish different types of responsibilities for the risk assessors. These responsibilities are usually specified in the terms of reference for the risk assessment and may include, for example:

- Review of the information provided in the LMO dossier, and in particular the information in the risk assessment provided by the applicant, if available;
- Identify any other relevant scientific information on the subject at hand, including previous risk assessments or new information that has come to light;
- Consider information gaps and scientific uncertainties and possible ways to address them;
- Conduct the risk assessment and prepare a report.

These actions are performed in a process that can be iterative. For example, it is possible that while the risk assessment is being conducted, a new piece of scientific information comes to light and reveals some information gaps that had not been previously identified. In such a case, it may be necessary to identify and engage additional sources of scientific expertise that should be included in the initial risk assessment panel or scientific advisory body.

In reviewing the LMO dossier or at any subsequent steps of the risk assessment, the CNA(s) or the risk assessor(s) may decide that further documentation is needed and may choose to request it from the applicant or to conduct or commission their own testing.

The risk assessor(s) in charge of leading the process is often responsible for the coordination of the expert panel or risk assessment team. Additionally they report the findings and disseminate relevant documents among other parties involved, including other stakeholders (see below), as appropriate, to ensure that information is shared properly and in a timely manner.

Responsibilities of the risk assessor(s)	
Parties to the Protocol shall ensure that they have procedures to protect confidential information as per Article 21 of the Protocol and in accordance with national legislation. As such, the risk assessor(s) is also required to respect any confidential business information indicated by the CNA taking into account that, according to the Protocol, the following information cannot be considered confidential: a) the name and address of the notifier; b) a general description of the living modified organism(s); c) a summary of the risk assessment highlighting the effects of the LMO on the conservation and sustainable use of biological diversity, taking also into account risks to human health; and d) any methods and plans for an emergency response. Once a scientific risk assessment is completed, the risk assessor(s) prepares a risk assessment report in accordance with the terms of reference established by the CNA. The report should be sufficiently detailed to provide the necessary scientific information to the decision makers (see Module 3).	

Roster of Experts on Biosafety	
To facilitate countries' access to relevant expertise when needed, the Parties to the Cartagena Protocol on Biosafety established the "Roster of Experts on Biosafety". The aim of this Roster is to "provide advice and other support, as appropriate and upon request, to developing country Parties and Parties with economies in transition, to conduct risk assessment, make informed decisions, develop national human resources and promote institutional strengthening, associated with the transboundary movements of living modified organisms". Information on individuals listed in the Roster of Experts on Biosafety is accessible through the BCH. As of March 2014, the Roster of Experts on Biosafety contained 159 experts from 45 countries.	
Stakeholder participation	
In the context of risk assessments of LMOs, stakeholders are all those with an interest or stake in biosafety, i.e. in the safe transfer, handling and use of LMOs in the country (UNEP-GEF, 2003). While there is no direct mention to stakeholder participation in Article 15 on Risk Assessment of the Protocol, Article 23 requires that Parties consult the public in the decision-making process regarding an LMO. Determining the extent to which the public and other stakeholders may be involved in the decision-making process is the prerogative of each regulatory framework. Some countries have a mechanism that enables public participation during the risk assessment and/or decision-making process. For example, one of the CNAs in New Zealand, the Environmental Protection Agency (EPA), opens LMO notifications to public consultation on its website.	

Module 3:

Conducting the Risk Assessment

Introduction

Risk assessments are intended to calculate or estimate the risk to a given target organism, system, or (sub)population, including the identification of uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system (WHO, 2004). In the context of biosafety, risk assessment can be defined as the process of estimating risks that may be associated with an LMO on the basis of what adverse effects may be caused, how likely the adverse effects are to occur, and the consequences should they occur.

The risk assessment process involves a critical review of available data for the purpose of identifying and possibly quantifying the risks resulting from, for example, natural events (flooding, extreme weather events, etc.), technology, agricultural practices, processes, products, agents (chemical, biological, radiological, etc.) and any activity that may pose threats to ecosystems, animals and/or people.

The objective of a risk assessment under the Cartagena Protocol "is to identify and evaluate the potential adverse effects of living modified organisms on the conservation and sustainable use of biological diversity in the likely potential receiving environment, taking also into account risks to human health" (Annex III).

he results of risk assessments of living modified organisms (LMOs) are typically used by decision-makers to make informed decisions regarding the approval, with or without conditions (e.g. requirements for risk management and monitoring strategies), or prohibition of a certain use of the LMO.

This module provides an introduction to risk assessment and considerations that may assist risk assessors in conducting risk assessments of LMOs that are consistent with Article 15 and Annex III of the Protocol.

Overview of the risk assessment methodology

In order to understand what is meant by risk assessment it is important to be familiar with the concepts of risk and hazard, and how these terms differ. The term "risk" does not have a single unambiguous definition but it is often defined as "the probability of harm". This is broadly understood as the likelihood that a harmful consequence will occur as the result of an action or condition.

Risk is often assessed through the combined evaluation of hazard and exposure.

- "Hazard", in the context of LMO risk assessment, is defined as the potential of an organism to cause harm to human health and/or the environment (UNEP, 1995).
- "Exposure" means the contact between a hazard and a receptor. Contact takes place at an exposure surface over an exposure period (WHO, 2004). In the risk assessment of LMOs, "exposure" can be understood as the route and level of contact between the likely potential receiving environment and the LMO or its products.

The exposure pathway from the hazard to the receptor and the possible exposure scenarios form important additional elements in understanding risk. Ascribing the probability and consequences of exposure of a receptor to the hazard characterizes the risk. All these elements must be evaluated to form an effective and useful risk assessment for specific scenarios (UNEP Division of Technology, Industry and Economics).

A simple example can be used to distinguish hazard from risk: acids may be corrosive or irritant (i.e. a hazard) to human beings. The same acid is a risk to human health only if humans are exposed to it without protection. Thus, the degree of harm caused by the exposure will depend on the specific exposure scenario. If a human only comes into contact with the acid after it has been heavily diluted, the risk of harm will be minimal but the hazardous property of the chemical will remain unchanged (EEA, 1998). "Exposure scenario" is a set of conditions or assumptions about sources, exposure pathways, amounts or concentrations of agent(s)involved, and exposed organism, system, or (sub)population (i.e., numbers, characteristics, habits) used to aid in the evaluation and quantification of exposure(s) in a given situation.

EXAMPLE: What is risk? What is Risk Assessment?

Overview of the risk assessment methodology

Risk assessment of LMOs can be divided into four main phases (WHO, 2004):

- Hazard identification: The identification of the type and nature of adverse effects that an LMO could cause to an organism, system, or (sub)population.
- Hazard characterization: The qualitative and/or quantitative evaluation of the nature of the adverse effects associated with an LMO.
- Exposure assessment: Evaluation of the exposure of the environment, including organisms, to an LMO or products thereof.
- Risk characterization: The qualitative and/or quantitative estimation, including attendant uncertainties, of the overall risk.

If risks are identified during the risk characterization step above, risk management strategies may be identified which may effectively prevent, control or mitigate the consequences of the adverse effects. As such, the risk assessment process often includes an additional step to identify a range of possible risk management strategies that could reduce the level of risk.

It is worth noting, however, that it is only during the decision-making process that a choice is made as to whether an identified risk is acceptable and whether or not risk management strategies are to be implemented (see more details on the identification of risk management strategies under step 5).

As a whole the risk assessment process can be highly iterative; meaning that one or several steps may need to be re-evaluated when, for instance, new information becomes available in an attempt to increase the level of certainty.

The methodologies for risk assessment of LMOs have evolved over the past few decades. At a conceptual level, the methodologies have been adapted from the existing paradigms for environmental risk assessment developed for chemicals and other types of environmental stressors (Hill, 2005). As a result, the terminology used within each methodology may vary. Familiarity with the different terms used in risk assessment enables a more direct comparison between the terminology used in Annex III and different risk assessment frameworks. It will also facilitate the interpretation of results from different risk assessments, for instance, for the same LMO.

FIGURE: Variation in terminology used to describe methodological components common to many risk assessment frameworks

Overarching issues

Quality and relevance of information

Risk assessors need to identify the information needed to conduct a risk assessment and understand how it will be used. Using and interpreting existing information, as well as identifying information gaps and understanding how to deal with scientific uncertainty are important factors during the risk assessment.

Considerations of the quality and relevance of information available for the risk assessment are important throughout the risk assessment process.

Scientifically sound methodologies should be determined and documented for testing any identified risk scenario. When assessment methods are well described, risk assessors and ubsequent reviewers are better equipped to determine whether the information used was adequate and sufficient for characterizing the risk.

EXAMPLE: Data acquisition, verification, and monitoring

An important question in a risk assessment is whether the information presented is of sufficient quality and relevance to characterize the risk posed by the LMO.

A number of issues are typically considered to ensure the quality and relevance of the information used as well as the outcome of the risk assessment. For example:

Criteria for the quality of scientific information:

- Information, including raw data, of acceptable scientific quality should be used in the risk assessment. Data quality should be consistent with the accepted practices of scientific evidence-gathering and reporting and may include independent review of the methods and designs of studies;
- Appropriate statistical methods should be used where appropriate, to strengthen the scientific conclusions of a risk assessment and be described in the risk assessment report. Risk assessments frequently use data generated from multiple scientific fields;

Reporting of data and methods should be sufficiently detailed and transparent to allow independent verification and reproduction. This would include ensuring the accessibility of data used by the risk assessors (e.g., the availability of relevant data or information and, if requested and as appropriate, sample material), taking into account the provisions of Article 21 of the Protocol on the confidentiality of information.

Quality and relevance of information	
Relevant information may be derived from a variety of sources such as existing scientific literature, experience and outcomes from previous risk assessments, in particular for the same or similar LMOs introduced in similar receiving environments, as well as new experimental data such as laboratory experiments (e.g. early tier toxicology testing), confined field experiments or other scientific observations. The relevance and level of detail of the information needed may vary from case to case depending on the nature of the modification of the LMO, on its intended use, and on the scale and duration of the environmental introduction.	*The relevance of information for the risk assessment:* • Information, including data, may be considered relevant if they are linked to protection goals or assessment endpoints, contribute to the identification and evaluation of potential adverse effects of the LMO, or if they can affect the outcome of the risk assessment or the decision; • Relevant information may be derived from a variety of sources such as new experimental data, data from relevant peer reviewed scientific literature, as well as data, experience and outcomes from previous risk assessments if regarded as of acceptable scientific quality, in particular for the same or similar LMOs introduced in similar receiving environments; • Information from national and international standards and guidelines may be used in the risk assessment, as well as knowledge and experience of, for example, farmers, growers, scientists, regulatory officials, and indigenous and local communities depending on the type of LMO, its intended use and the likely potential receiving environment;* • The information that is relevant to perform a risk assessment will vary from case to case depending on the nature of the modification of the LMO, on its intended use, and on the scale and duration of the environmental introduction. In cases of environmental releases whose objective is to generate information for further risk assessments and where exposure of the environment to the LMO is limited, such as for some early-stage experimental releases and trials, less information may be available or required when performing the risk assessment. The uncertainty resulting from the limited information available in such cases may be addressed by risk management and monitoring measures. *Additional considerations with regard to scientific information:* • The process of risk assessment may give rise to the need for further relevant information about specific subjects, which may be identified and requested during the assessment process; • Whether independent experts with the relevant background in the different scientific disciplines are available to conduct risk assessments or to provide input into the risk assessment process. * Risk assessments can be found, inter alia, in the BCH and ICGEB.

Identification and consideration of uncertainty	
Uncertainty is an inherent and integral element of scientific analysis, and its consideration is undertaken throughout the whole risk assessment process. The risk assessment methodology as set out by the Cartagena Protocol states that "where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment". (4) Although uncertainty may, in some cases, be addressed by requesting additional information, the necessary information may not always be available or new uncertainties may arise as a result of the provision of additional experimental data. The golden rule during the risk assessment of an LMO is to request additional information that is relevant to the overall evaluation of risk and will facilitate the decision making. Thus, it is important to consider and analyze, in a systematic way, the various forms of uncertainty (e.g. types and sources) that can arise at each step of the risk assessment process. ***EXAMPLE: Scientific uncertainty***	Uncertainty is an inherent and integral element of scientific analysis and risk assessment. According to the Protocol, "where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies or monitoring the living modified organism in the receiving environment". Whether and to what extent there is scientific uncertainty is therefore critical in the context of risk assessment. There is no internationally agreed definition of "scientific uncertainty", nor are there internationally agreed general rules or guidelines to determine its occurrence. The issue of uncertainty is dealt with – sometimes differently – in each international instrument incorporating precautionary measures*. Considerations of uncertainty strengthen the scientific validity of a risk assessment. These include considerations of its source and nature, and focuses on uncertainties that can have a significant impact on the conclusions of the risk assessment. * An Explanatory Guide to the Cartagena Protocol on Biosafety, paragraphs 52-66.

Identification and consideration of uncertainty	
Uncertainties may arise from: (i) lack of information, (ii) incomplete knowledge, and (iii) biological or experimental variability, for example, due to inherent heterogeneity in the population being studied or to variations in the analytical assays. Uncertainty resulting from lack of information includes, for example, information that is missing and data that is imprecise or inaccurate (e.g., due to study designs, model systems and analytical methods used to generate, evaluate and analyse the information) (SCBD, 2012). If the level of uncertainty changes during the risk assessment process (e.g. by provision of new information), an iteration of parts or the entire risk assessment process may be needed. It is important to note that while scientific uncertainty is considered during the risk assessment process and the results of uncertainty considerations may be reported it is, ultimately, the responsibility of the decision-makers to decide how to use the information in conjunction with the principals of the precautionary approach when making a decision on an LMO.	For each identified uncertainty, the nature of the uncertainty may be described as arising from: (i) lack of information, (ii) incomplete knowledge, and (iii) biological or experimental variability, for example, due to inherent heterogeneity in the population being studied or to variations in the analytical assays. Uncertainty resulting from lack of information includes, for example, information that is missing and data that is imprecise or inaccurate (e.g., due to study designs, model systems and analytical methods used to generate, evaluate and analyze the information). In some cases more information will not necessarily contribute to a better understanding of potential adverse effects, therefore risk assessors should look to ensure that any further information requested will contribute to better evaluations of the risk(s). Although uncertainties originating from lack of information may be reduced by further research, uncertainties arising from incomplete knowledge or from inherent variability may be irreducible. In such cases, instead of reducing uncertainty, the provision of additional information may actually give rise to new uncertainties. The various forms of uncertainty are considered and described in each step of the risk assessment. In addition, when communicating the results of a risk assessment, it is important to describe, quantitatively or qualitatively, what impact uncertainty may have on the estimated level of risk and on the conclusions and recommendations of the risk assessment. In cases where the nature of the uncertainty implies that it cannot be addressed through the provision of more data during the risk assessment, where necessary, it may be dealt with by risk management and/or monitoring in accordance with paragraphs 8(e) and 8(f) of Annex III to the Protocol (see step 5 and Part III).

Planning phase

Establishing the context and scope	
When the regulatory process of a country triggers the need for a risk assessment, it usually results in a request from the competent authority to the risk assessor(s). This request includes the scope of the risk assessment to be carried out as well as some important elements that will set the context of the risk assessment. In a typical case-by-case scenario, in accordance with the Cartagena Protocol, these elements will include at a minimum: the LMO(s), its(their) specific use(s) and, in cases of introduction into the environment, the likely potential receiving environment(s) where the LMO may be released and establish itself. As such, the case-by-case approach does not allow an existing risk assessment to be applied "as is" to different LMOs, uses or receiving environments. Nevertheless, a risk assessment carried out on a case-by-case basis most often takes into account relevant knowledge and experience gained in previous risk assessments. In practice, if a risk assessor is faced with a request by the Competent National Authorities (CNA) to conduct or review a risk assessment that does not follow the case-by-case principle, the risk assessor recommends to the CNA that a new risk assessment be carried out with a scope that is specific to the case under consideration (i.e. the LMO, its specific use and the likely potential receiving environment).	Risk assessments are carried out on a case-by-case basis in relation to the LMO, its intended use and the likely potential receiving environment. Each risk assessment starts by establishing its context and scope in a way that is consistent with the country's protection goals, assessment endpoints, risk thresholds, risk management strategies and policies. Establishing the context and scope for a risk assessment, in line with the country's policies and regulations, may involve an information-sharing and consultation process with risk assessors, decision-makers and various stakeholders prior to conducting the actual risk assessment, to identify protection goals, assessment endpoints and risk thresholds relevant to the assessment. It may also involve identifying questions to be asked that are relevant to the case being considered. The risk assessors should, at the outset of the process, have knowledge of national requirements for risk assessment and criteria for acceptability of risks. They may also use questions or checklists designed for the case under consideration to assist in the subsequent steps. Some risk assessment frameworks combine the process of establishing the context and scope of the risk assessment with the identification of potential adverse effects associated with the modifications of the LMO into a single step called "Problem formulation" (see step 1).

[note: the location of the text highlighted in gray was changed slightly in relation to the original document for a better alignment]

Establishing the context and scope	
Protection goals for the conservation and sustainable use of biodiversity, may be defined in national, regional and international policies. In setting the context of a risk assessment, these goals may be relevant to the identification and selection of appropriate assessment endpoints and to determining which methodology will be used in the risk assessment process. Understanding the contribution of national, regional and regulatory policies in setting the context of the risk assessment is part of the preparatory work for a risk assessment as seen in Module 2. After consideration of the protection goals, the risk assessment of a particular LMO proceeds to establishing the scope in order to define the extent and the limits of the risk assessment process. This phase usually consists of at least three main actions: (i) selecting relevant assessment endpoints or representative species on which to assess potential adverse effects; (ii) establishing baseline information; and (iii) when possible, establishing the appropriate comparator(s). Although these actions are described here as separate activities, in practical terms, this is an iterative process where the risk assessors will usually draw on the results of each action to inform the subsequent actions until all their elements have been considered sufficiently enough to enable the risk assessment to proceed.	

Establishing the context and scope	
	Several points may be taken into consideration when estaclisji, as appropriate, that are specific to the Party involved* and to the particular risk assessment. These include: • Existing environmental and health policies and strategies based on, for instance: i. Regulations and international obligations of the Party involved; ii. Guidelines or regulatory frameworks that the Party has adopted; and iii. Protection goals, assessment endpoints, risk thresholds and management strategies as laid down, for instance, in relevant legislation of the Party; • Intended handling and use of the LMO, including practices related to the use of the LMO, taking into account user practices and habits; • The nature and level of detail of the information that is needed (see above), which may, among other things, depend on the biology/ecology of the recipient organism, the intended use of the LMO and its likely potential receiving environment, and the scale and duration of the environmental exposure (e.g., whether it is for import only, field testing or for commercial use). For small-scale releases, especially at early experimental stages or in the early steps of environmental releases of LMOs that are conducted in a step-wise manner, the nature and detail of the information that is required or available may differ compared to the information required or available for large scale or commercial environmental release; • Identification of methodological and analytical requirements, including requirements for review mechanisms, that must be met to achieve the objective of the risk assessment as specified, for instance, in guidelines published or adopted by the Party that is responsible for conducting the risk assessment (i.e., typically the Party of import according to the Protocol); • Experience and history of use of the non-modified recipient organism, taking into account its ecological function; • Approaches for describing potential adverse effects of the LMO and terms used for describing the likelihood (step 2), the magnitude of consequences (step 3) and risks (step 4), and the acceptability or manageability of risks (step 5). * See Protocol provisions with regard to whose responsibility it is to ensure that risk assessments are carried out

Selecting relevant assessment endpoints or representative species

The purpose of an assessment endpoint or of representative species is to provide a measure that will indicate whether or not the LMO may cause an adverse impact on a protection goal. In order to be useful, the selected assessment endpoints or characteristics of the representative species should be specific and measureable.

Assessment endpoints or species representative of important ecological functions[(5)] or roles should be selected on a case-by-case basis. The complexity of ecosystems and the large number of potential candidates add to the challenges in selecting the appropriate assessment endpoints in ecological systems. Some important criteria for the selection of assessment endpoints to be used in the risk assessment of LMOs may include, for example: (i) their relevance to the protection goals; (ii) a well-defined ecological function; (iii) accessibility to measurement; and (iv) level of potential exposure to the LMO.

Identifying assessment endpoints or representative species that are relevant within the context of the likely potential receiving environment allows the risk assessor(s) to focus on interactions that are likely to occur. Moreover, risk scenarios may be also formulated to include assessment endpoints or representative species that are not present in the likely potential receiving environment but may, nevertheless, be indirectly exposed to the LMOs. This could occur, for example, if a third species, which is sexually compatible with the LMO and the representative species, has a distribution area that overlaps with the distribution areas of the former two providing an indirect exposure pathway between them.

EXAMPLE: Common problems in selecting assessment endpoints

EXAMPLE: Questions asked when selecting representative species for assessing effects of Bt plants on non-target organisms

Establishing the baseline	
In risk assessment, the baseline is a description or a measurement of existing conditions of an environment, or its attributes or components without the LMO under consideration and taking into account different practices in use (e.g., agricultural practices). The baseline description or measurement may provide quantitative (e.g., number of organisms, variability of abundance) and/or qualitative information about the receiving environment as a reference for estimating effects of the LMO or its use including, if applicable, information on the assessment endpoints. Baselines can refer to, for instance, a particular environment or health conditions of a population. Baselines are established with the aim of having descriptive and/or measurable information on any element of the likely potential receiving environment that is considered relevant in assessing the impacts from the introduction of the LMO, including considerations on possible impacts on human health. In practice, if relevant assessment endpoints or representative species are selected, the baseline data will consist of data that establishes the conditions of these endpoints or species before the introduction of the LMO in question. ***EXAMPLE: Baseline information***	

The choice of comparators

As seen in previous slides, a comparative approach is one of the general principles of risk assessment as set out in Annex III to the Protocol, where risks associated with the LMO "should be considered in the context of the risks posed by the non-modified recipients or parental organisms in the likely potential receiving environment".

Using a comparator, i.e. non-modified recipients or parental organisms of the LMOs used as an element to establish the basis for a comparative assessment in accordance with Annex III, helps a risk assessor to identify the novel characteristics of the LMO and assess if the LMO presents a greater, lesser or equivalent risk compared to the non-modified recipient organism that is used in a similar way and in the same environment.

In some circumstances, choosing an appropriate comparator(s) can be a challenge. This may happen, for example, in the case of LM crops that are tolerant to abiotic stress if the non-modified recipient or parental organisms are not capable of growing in the receiving environment. In extreme situations, when a suitable comparator cannot be grown under the same conditions and in the same or similar receiving environment as the LMO, it may be necessary to treat the LMO as a novel species in that environment (i.e. introduced species). This means that the characterization of the LMO (see under step 1) will focus not only in the novel genotypic and phenotypic characteristics(6) resulting from the genetic modification, but rather on the characterization of an entire new genotype in the particular receiving environment.

Risks associated with an LMO should be considered in the context of the risks posed by the non-modified recipients or parental organisms in the likely potential receiving environment.

A comparative approach aims at identifying changes between an LMO and its comparator(s) that may lead to adverse effects. The choice of comparators can have large effects on the relevance, interpretation and conclusions drawn from the risk assessment process. Therefore, the one or more comparators that are chosen should be selected on the basis of their capacity to generate information that is consistent and relevant for the risk assessment.

To account for variation due to interaction with the environment, the LMO and its comparator(s) should ideally be evaluated at the same time and location, and under the same environmental conditions.

Choosing the appropriate comparator(s) may, in some cases, be difficult or challenging.

[note: the location of the text highlighted in gray was changed slightly in relation to the original document for a better alignment]

The choice of comparators	
The ideal comparator is the closest non-modified genotype to the LMO, i.e. (near-)isogenic lines[7]. However, (near-)isogenic lines are not always available and the choice of appropriate comparators may be guided by policies or guidelines adopted by the country undertaking the risk assessment (e.g. EFSA, 2011). Moreover, depending on the context, the step of the risk assessment and question being asked, a risk assessor may also choose to consider similar or related non-modified genotypes as useful comparators. Related management practices and experience with similar non-modified organisms may also be helpful. For example, when considering the risk assessment for an insect resistant LM crop, a risk assessor may wish to consider, amongst other things, the available experience with pest control practices applied to non-modified organisms of the same species (e.g. use of spores from Bacillus thuringiensis as pesticides).	Some risk assessment approaches use a non-modified genotype with a genetic background as close as possible to the LMO being assessed, e.g., a (near-) isogenic line as the primary choice of comparator. In such risk assessment frameworks where the use of a (near-)isogenic non-modified recipient organism as the comparator is required, additional comparators may prove useful depending on the biology of the organism and types of modified traits under assessment. In practice, the (near-)isogenic non-modified organism is used in step 1 and throughout the risk assessment. When the likelihood and potential consequences of adverse effects are evaluated, broader knowledge and experience with additional comparators such as defined non-modified reference lines may also be taken into consideration, as appropriate, along with the non-modified recipient organism. Results from experimental field trials or other environmental information and experience with the same or similar LMOs in the same or similar receiving environments may also be taken into account. In other risk assessment approaches, the choice of an appropriate comparator will depend on the specific LMO being considered, the step in the risk assessment and on the questions that are being asked. In some cases, the non-modified recipient organisms or the parental organisms alone may not be sufficient to establish an adequate basis for a comparative assessment. In such cases, additional approaches and/or comparators may be necessary (for concrete examples and more guidance, please refer to Part II of this Guidance).

Conducting the risk assessment

Introduction

Conducting the risk assessment involves synthesizing what is known about the LMO, its intended use and the likely potential receiving environment to establish the likelihood and consequences of potential adverse effects to biodiversity, taking into account human health, that result from the introduction of an LMO.

Neither the Protocol nor this Manual makes a distinction between the various types of introductions into the environment, such as releases for experimental purposes or releases for commercial purposes. However, the nature and level of detail of the information needed to conduct the risk assessment will vary depending on the intended use of the LMO (e.g. type of release), the LMO itself and the likely potential receiving environment.

The following slides will address the steps of the risk assessment methodology described in paragraph 8 of Annex III to the Protocol. These steps describe a structured and integrated process whereby the results of one step are relevant to subsequent steps.

Additionally, the risk assessment process may need to be conducted in an iterative manner, whereby certain steps may be repeated or re-examined to increase or re-evaluate the reliability of the risk assessment. If during the process, new information arises that could change the outcome of a step, the risk assessment may need to be re-examined accordingly.

To fulfill the objective under Annex III of the Protocol, as well as provisions under other relevant articles, a risk assessment is conducted in steps, in an integrated process and in an iterative manner, as appropriate. Paragraph 8 of Annex III describes the key steps of the risk assessment process. Paragraph 9 of Annex III lists and describes points to consider in the process for risk assessment of LMOs depending on the particular case.

The steps of risk assessment under the Protocol are similar to those used in other risk assessment frameworks. Although the terminology may differ between the various approaches, in general terms, risk assessment is defined as a science-based process that includes at least the following common components (corresponding to the steps 1 to 4 respectively): “hazard identification”, “exposure assessment”, “hazard characterization”, and “risk characterization”.

In this section, the steps indicated in paragraph 8(a)-(e) of Annex III are described in further detail and points to consider are provided for each step. Some points to consider are taken from paragraph 9 of Annex III. Additional points to consider were added on the basis of commonly used methodologies of LMO risk assessment and risk management insofar as they were in line with the principles of Annex III. The relevance of each point to consider will depend on the case being assessed. The guidance provided below on the steps in risk assessment is not exhaustive, thus additional guidance and points to consider may be relevant, as appropriate. Lists of background documents relevant to each section are provided through the links.

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
The first step of the risk assessment is "an identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects on biological diversity in the likely potential receiving environment, taking into account risks to human health". [8] What constitutes an "adverse effect" (also referred to as "damage" or "harm") will depend on the context and scope of the risk assessment taking into account, as appropriate, the specific protection goals as seen above. ***EXAMPLE: Potential adverse effects*** ***EXAMPLE: Risks*** ***EXAMPLE: Potential adverse effects*** ***EXAMPLE: Topics of concern***	***Rationale*** The purpose of this step is to identify changes in the LMO, resulting from the use of modern biotechnology, that could cause adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health. The potential adverse effects may be direct or indirect, immediate or delayed. The question that risk assessors ask in this step is what adverse effects could occur, why and how. This step is very important in the risk assessment process as the questions raised will determine what risk scenarios are considered in all subsequent steps. This step may also be referred to as "hazard identification" – the difference between the concepts of "hazard" and "risk" is important and must be understood by the risk assessor. In many cases, this step is performed as part of a problem formulation process when establishing the context and scope of the risk assessment. In that case, this step is not limited to the identification of hazards, but also takes into account protection goals and appropriate assessment endpoints. Whether step 1 and "establishing the context and scope" are done in parallel or in sequence, together these actions are among the most important in a risk assessment as they form the basis for the subsequent steps.

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
The genotypic and phenotypic characterization of an LMO provides the basis for identifying differences, both intended and unintended, between the LMO and its recipient or parental organism(s). Molecular analyses may be performed to characterize the products of the modified genetic elements, as well as of other genes that may have been affected by the modification. Data on specific expression patterns may be relevant for risk assessment in order to determine exposure, and may also include data confirming the absence of gene products, such as RNA and proteins, different from those originally intended. For example, in the case where the gene product (i.e. the RNA or protein that results from the expression of a gene) is intended to function only in a specific tissue, data may be used to confirm its specificity in that tissue and demonstrate its absence in other tissues. Other phenotypic data are often presented to indicate that the LMO is behaving as anticipated. This could include data on reproductive characteristics, alterations in susceptibility to pests and diseases or tolerance to abiotic stressors, etc. Once the potential adverse effects have been identified, the risk assessment proceeds to estimating the likelihood and consequences of these effects. To this end, developing risk scenarios may in some cases provide a useful tool.	In this step, a comparison of the LMO should be considered in the context of the non-modified recipient or parental organisms in the likely potential receiving environment, taking into consideration the new trait(s) of the LMO (see 'The choice of comparators' in the chapter entitled 'Planning Phase of the Risk Assessment'). The novel characteristics of the LMO to be considered can be described in genotypic and phenotypic terms. These include any changes in the LMO, ranging from the nucleic acid (including any deletions), to gene expression level to morphological changes.

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
A risk scenario may be defined as a sequence of events with an associated probability and consequence. In the context of risk assessment of LMOs, a risk scenario may be explained as a scientifically supportable chain of events through which the LMO might have an adverse effect on an assessment endpoint. A well-defined risk scenario should be scientifically plausible and allow the assessor to identify information that is necessary for the assessment of risks. Although some risk scenarios may appear as obvious (e.g. potential for insect resistant plants to affect insect herbivore populations), it is always useful to identify the risk scenarios fully. Clear and well-defined risk scenarios can also contribute to the transparency of a risk assessment because they allow others to consider whether or not the subsequent steps of the risk assessment have been adequately performed and facilitate the consideration of possible strategies to manage the identified risks. A common challenge in generating a well-defined risk scenario is to choose representative species that would be exposed to the LMO. This is why an exposure assessment should be considered when selecting assessment endpoints. ***EXAMPLE: A risk scenario***	In this step, risk assessors identify scientifically plausible scenarios and risk hypotheses to predict if the LMO could have an adverse effect on the assessment endpoints. In doing so, risk assessors analyse what novel characteristics of the LMO, as well as its transfer, handling and use, could give rise to adverse effects in an interaction with the likely potential receiving environment. For example, if the protection goal is maintenance of biodiversity, a risk hypothesis could assess what novel characteristics of the LMO might affect specific “targets” such as a component of the food web or the population size of certain species in the likely potential receiving environment. The targets are called assessment endpoints, and their unambiguous specification is crucial to focus the risk assessment.

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
When establishing risk scenarios several considerations may be taken into account. These may include: (i) gene flow followed by introgression of the transgene in species of interest; (ii) toxicity to non-target organisms; (iii) allergenicity; (iv) multi-trophic interactions and indirect effects; and (v) resistance development. The following slides explain some of these considerations in more detail.	It is important to define a causal link or pathway between a characteristic of the LMO and a possible adverse effect, otherwise the risk assessment may generate information that will not be useful for decision-making (see also steps 2 and 3). […] The LMO may cause adverse effects which may be direct or indirect, immediate or delayed, combinatorial or cumulative, as well as predicted or unpredicted. For example, an adverse effect may also be caused by changes in the expression levels of endogenous genes as a result of the genetic modification or by combinatorial effects of two or more genes, gene products or physiological pathways. […] Depending on the LMO, its intended use and the likely potential receiving environment, possible changes that could lead to adverse effects may include, but are not limited to, the potential of the LMO to: (i) affect non-target organisms, (ii) cause unintended effects on target organisms, (iii) become persistent or invasive or develop a fitness advantage in ecosystems with limited or no management, (iv) transfer genes to other organisms/populations, and (v) become genotypically or phenotypically unstable.

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
Gene flow followed by introgression of the transgene in species of interest – "Gene flow" is the transfer of genetic material from one organism to another by vertical or horizontal gene transfer; or the movement of an organism from one environment to another. In the case of plants, vertical gene flow may occur even between organisms that are located far apart since pollen can be carried across large distances by the wind or insects, for instance. "Introgression" is the movement of a gene or genetic element from one species into the gene pool of another species or population, which may result in a stable incorporation or some fertile offspring. Gene flow followed by introgression from an LMO to non-modified organisms may or may not be considered an adverse effect depending on the protection goals. The potential for gene flow is first evaluated by investigating if sexually compatible species are present in the likely potential receiving environment. If sexually compatible species are present, there is a possibility of gene flow from the LMO to these species. Whether or not the modified genetic elements can potentially introgress into the population of the sexually compatible species will be largely determined by the biology of the recipient organism and of the LMO itself (see considerations regarding the likelihood and consequences of gene flow and introgression in steps 2 and 3). "Vertical gene transfer" refers to the transfer of genetic material from one organism to its offspring via asexual, parasexual or sexual reproduction. Also referred to as "vertical gene flow". "Horizontal gene transfer" refers to the transfer of genetic material from one organism to another through means other than inheritance from parent to offspring (i.e., vertical). ***EXAMPLE: Gene flow to conventional crops and distant relatives through "genetic bridges"***	

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
Toxicity to non-target organisms – The potential for an introduced gene product to be toxic to organisms in the environment is typically addressed by controlled exposure in the environment or by direct toxicity testing, or by a combination of the two. Non-target organisms may include, for instance, herbivores, natural enemies (e.g. parasitoids and predators), pollinators and pollen feeders, soil (micro-)organisms and weeds. The need and extent of toxicity tests will depend on characteristics of the LMO and the level of exposure of other organisms to the LMO. If toxicity testing is needed, it typically follows a sequential series of tiered tests. Early tier studies involve highly controlled laboratory environments where representative or surrogate test species are exposed to high concentrations of the gene product being studied (i.e. worst case exposures) to determine if there are any toxic effects. If toxic effects are observed in early tier tests or if unacceptable uncertainty exists, e.g. regarding effects in multi-throphic interactions (see below), more realistic conditions representative of field-level exposures can be tested to determine the extent of the risk. The gene products of the modified genetic elements in LMOs may be produced in very small quantities thus may be difficult to isolate in the amounts required for toxicity testing. If this is the case, and it is determined that toxicity tests are required, the risk assessor may consider results from tests using gene products obtained from alternate (surrogate) sources (e.g. bacterial expression systems or the organism from which the transgene was derived) provided that these gene products are chemically and functionally equivalent.	

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
Allergenicity – Allergies are a type of adverse immunological response that affect individuals who are predisposed to certain types of substances (i.e. allergens). Allergens are often proteins or peptides. In considering allergenicity caused by LMOs, it is important to take into account the exposure to proteins newly expressed by the LMO, including some variants of these proteins (e.g. structural variants of proteins having sometimes very few difference(s) in amino acids composition – or no difference in amino acids composition but carrying slightly different saccharide branches – that may display different allergenic properties through differences in spatial structure) that may be produced uniquely by the LMO. As a consequence, some allergenicity studies must be carried out with proteins isolated from the LMO itself, and not obtained from an alternate (surrogate) source such as a bacterial expression system. It is also possible that allergens known to exist in the recipient or parental organism(s) are produced in higher amounts, for example by over-expression of the gene that encodes a protein that is known to be a common allergen. ***FIGURE: Assessment of the allergenic potential of foods derived from modern biotechnology***	

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
Multi-trophic interactions and indirect effects – "Multi-trophic interactions" involve more than two trophic levels in a food web. They are an important concept in ecology and occur when a change at one trophic level indirectly affects trophic levels which are more than one step away. Consideration of tri-trophic interactions and indirect effects may be relevant to biodiversity protection goals. Observations and experimentation to identify such effects are challenging because of the complexity of ecological interactions, the difficulty of establishing causality between observed variation and treatment effects (e.g. the presence of the modified genetic element or its products), and natural variability in populations over time. Moreover, in a food chain (or food web), effects at the trophic levels may become observable only at a later stage. ***EXAMPLE: Multi-trophic interactions and indirect effects***	

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
Resistance development – The extensive use of herbicides and insect resistant LM crops has the potential to result in the emergence of resistant weeds and insects. Similar breakdowns have routinely occurred with conventional crops and pesticides. Several weed species have developed resistance to specific herbicides which are extensively used in combination with herbicide-resistant LM crops. Insect-resistant Bt-crops similarly could lead to the emergence of Bt-resistant insects (FAO, 2004). The extent of the adverse effect and possible consequences of the insurgence of resistant weeds and insects should be thoroughly considered in a risk assessment. Some regulatory frameworks require that risk management strategies are identified in order lower the risk of resistance development. ***EXAMPLE: Insect resistance and herbicide tolerance management plans***	

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects

Elements of a case-by-case risk assessment of LMOs

The case-by-case approach in risk assessment is based on the premise that risks that may arise from the release of an LMO depend on three main elements: (i) the LMO itself; (ii) the likely potential receiving environment; and (iii) the intended use of the LMO in question. In order to identify and assess risks, each of these elements needs to be characterized in a concerted manner and as appropriate for the specific risk assessment. Moreover, it is important to note that while these three elements may be sufficient to establish the boundaries of a risk assessment, potential adverse effects may extend past these elements, for instance, beyond the likely potential receiving environment and the intended use(s) of the LMO.

The information required for each of these elements in a risk assessment may vary in nature and level of detail from case to case. The following sections provide examples of information that may be relevant for the characterization of each element above. These sections include several of the "points to consider" as indicated in paragraph 9 of Annex III of the Protocol.

A large portion of the information listed here is usually included in the LMO request triggering the risk assessment. The risk assessors can determine whether or not the information provided is sufficient and adequate for conducting a scientifically sound risk assessment. If needed, they can obtain additional information by, for instance, carrying out their own investigation or requesting it from the applicant.

EXAMPLE: The case-by-case approach

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
Living modified organism – *Characterization of the recipient organism* In order to identify whether or not the LMO possesses characteristics that may cause potential adverse effects (see above), it is first necessary to have information about the non-modified recipient organism (or parental organisms). For many LMOs, the biology of the recipient organism will strongly influence the potential interactions of the LMO in the receiving environment. Information on the recipient organism is therefore essential as it will help the risk assessor identify the exposure, its scenarios and, ultimately, if any risk is posed by an LMO. The information that is needed for the characterization of the recipient organism will vary depending on each case. For example, the nature and detail of information about the recipient organism that is required may differ between small-scale releases for experimental purposes and large-scale commercial releases. It normally includes the biological and reproductive characteristics of the recipient organism that can be important for determining the potential exposure of other organisms, such as predators, prey, competitors or pathogens, to the LMO in question in the likely potential receiving environment. For many species of LMOs, information on the recipient organism can be found in biology documents, such as those published by the Organization for Economic Co-operation and Development (OECD) and the Canadian Food Inspection Agency (CFIA). The LMO will, in most cases, share most of its genetic characteristics with its actual recipient organism (i.e. the one used in the modification) rather than with other genotypes of the same species. Thus, it is also important to consider, whenever possible, comparative data from the actual non-modified recipient organism (see the section on “The choice of comparators”).	

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects

Living modified organism – *Characterization of the recipient organism* Information about recipient organism to be considered may include: Taxonomic status – This information is useful for identifying the recipient organism and ensuring that information provided and cited during the assessment pertains to the organism for which the assessment is being carried out. Typically, the taxonomic status includes the scientific name (i.e. genus and species, for example, Zea mays) and information about the taxonomic family (e.g. Poaceae). This may also include other information used to further classify (e.g. sub-species, variety, strain) or differentiate the recipient or parental organism(s) (e.g. ploidy level or chromosome number). Common name – The familiar or colloquial names for the recipient organism that may be commonly used in the country of introduction and in international trade may be useful for finding information relevant to the biology of the organism. Caution is recommended when using information about recipient organism when only common names (versus the scientific name) are used because the same common name can be applied to more than one species. Biological characteristics – Information on the biological characteristics of the recipient organism, such as the production of endogenous toxins and allergens, its reproductive biology, dispersal of seeds and vegetative propagules, and growth habits, are also important points for consideration.	*Points to consider regarding characterization of the LMO:* (a) Relevant characteristics of the non-modified recipient organism, such as: (i) its biological characteristics, in particular those that, if changed or resulting in an interaction with the new gene products or traits of the LMO, could lead to changes that may cause adverse effects; (ii) its taxonomic relationships; (iii) its origin, centres of origin and centres of genetic diversity; (iv) ecological function; and (v) whether it is a component of biological diversity that is important for the conservation and sustainable use of biological diversity in the context of Article 7(a) and Annex I of the Convention;

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
Living modified organism – *Characterization of the recipient organism (continued...)* Origin – The origin of the recipient organism refers to its place of collection and may be important because populations within a species (e.g., variety, strain, isoline, etc.) may have significantly different characteristics. For domesticated species, this may be supplemented with a pedigree map where available. Centres of origin and centres of genetic diversity – Knowledge of the centre(s) of origin and genetic diversity can provide information on the presence of sexually compatible species and the likelihood of ecological interactions in the receiving environment. In the absence of more specific information, the centre of origin can also offer insight into the biology of the species (e.g. habitats to which the species is adapted). Habitat where the recipient or parental organism(s) may persist or proliferate – Information about the ecosystems and habitats (e.g. temperature, humidity, altitude, etc) where the recipient organism is known to be native and where it may have been introduced and is now established provides useful baseline information. This allows the risk assessors to understand the range of habitats in which the species exists, the range of behaviours exhibited in those habitats, and how characteristics of the species determine the range of habitats where it can persist or proliferate. This information can be very valuable in determining the likely potential receiving environment and, consequently, the level of exposure to the LMO. Likewise, the ecological characteristics of the recipient organism will help determine which organisms in the likely potential receiving environment are likely to come into contact, either directly or indirectly, with the LMO and will help determine the exposure pathways. For more details on the type of information that may be useful, see the section "Likely potential receiving environment". The history of use can be very valuable as well. If an organism persists in heavily managed environments (e.g. agriculture, sylviculture or recreationally managed land) then this will provide information about the conditions necessary for its survival. It may also provide direct indications of how the LMO will behave in other managed environments.	

<table>
<tr><th colspan="2">Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects</th></tr>
<tr><td>Living modified organism – Description of the genetic modification

Information on the genetic material that was introduced or modified, as well as the method used for the genetic transformation is useful in identifying novel properties of the LMO such as, what new gene products are expressed and which of the endogenous genes of the recipient or parental organism(s) may be affected by the genetic modification.

Typically the description of the genetic modification includes information on (i) the “donor organism(s)” or the source of the inserted genetic element(s); (ii) characteristics of each modified genetic element, including their intended and known biological function(s); (iii) the vector used, if applicable; and (iv) the transformation method.

The next slides contain a brief explanation on each of these points.</td><td>Points to consider regarding characterization of the LMO:

[...]

(b) Characteristics related to the transformation method, including the characteristics of the vector such as its identity, source or origin and host range, and information on whether the transformation method results in the presence of (parts of) the vector in the LMO, including any marker genes;

(c) Relevant characteristics of the genes and of other functional sequences, such as promoters, that have been inserted into the LMO (e.g., functions of the gene and its gene product in the donor organism with particular attention to characteristics in the recipient organism that could cause adverse effects);

(d) Molecular characteristics of the LMO related to the modification, such as characteristics of the modified genetic elements; insertion site(s) and copy number of the inserts; stability, integrity and genomic organization in the recipient organism; specificity of the genetic elements (e.g., transcription factors); levels of gene expression and intended and unintended gene products;

(e) Genotypic (see point (d) above) and phenotypic changes in the LMO, either intended or unintended, in comparison with the non-modified recipient, considering those changes that could cause adverse effects. These may include changes in native/endogenous gene expression and regulation at the transcriptional, translational and post-translational levels.</td></tr>
</table>

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
Living modified organism – *Description of the genetic modification (continued...)* Donor organism(s) – The relevant information on the donor organism(s) includes its taxonomic status, common name, origin and relevant biological characteristics. Modified genetic elements – The relevant information on the modified genetic elements encompasses the name, sequence, function and other characteristics of all the nucleic acid sequences that were inserted, deleted or modified in the LMO. These include not only the target gene(s) but also, for example, all marker genes, regulatory sequences, and any non-coding DNA. If available, a history of use may be important with regards to potential toxicity or allergenicity of the gene products derived from the donor organism. If the genetic elements originate from a donor organism that is known to be a pest or pathogen it is also relevant to know if and how these elements contribute to the pest or pathogenic characteristics. Vector – In molecular biology, a vector is a nucleic acid molecule used as a vehicle to transfer foreign genetic material into a cell. If a vector, for example a plasmid, was used for the transformation, relevant information includes its identity, source or origin, and its host range. Transformation method – Specifying the method that was used in the transformation (e.g. Agrobacterium mediated, particle gun, etc.) is also relevant when describing the genetic modification. Depending on the transformation method, parts of the vector(s) may also be incorporated into the genome of the newly developed LMO. Characteristics of the modification – This refers to information about whether or not the inserted or modified genetic elements are present and functioning as expected in the LMO. Normally this involves confirmation that the DNA insert or modified genetic element is stable in the genome of the LMO. Information such as the insertion site in the genome of the recipient or parental organism(s), cellular location of the insert (e.g. chromosomal, extrachromosomal, or chloroplast DNA), its mode of inheritance and copy number may also be relevant.	

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
Living modified organism – *Identification of the LMO* With regard to the identification of the LMO, the following are important points to consider: Unique identifiers – A Unique identifier is a code provided by the LMO developer to a transformation event derived from recombinant DNA techniques to enable its unequivocal identification. Each unique identifier is made up of a sequence of 9 alphanumeric digits, for example MON-89788-1, assigned according to the OECD guidance document (OECD, 2006). Detection and identification methods – The availability of methods for detection and identification of the LMO may be considered as well as their specificity, sensitivity and reliability. This information may be relevant not only for assessing risks but also when considering possible monitoring and risk management strategies (see step 5). Some regulatory frameworks require a description of such methods as a condition for regulatory approval in order to ensure the tools to assist with monitoring and risk management are available. The Biosafety Clearing-House of the Cartagena Protocol maintains an LMO registry containing, amongst other things, information on unique identifiers, molecular characteristics and available detection methods for the LMOs addressed in countries' decisions. ***EXAMPLE: Detection and identification method criteria***	

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects

Likely potential receiving environment(s)

The Protocol calls for the characterisation of the "likely potential receiving environment" of an LMO. According to UNEP (1995), the "potential receiving environment" is the range of environments (ecosystem or habitat, including other organisms) which are likely to come in contact with a released organism due to the conditions of the release or the specific ecological behaviour of the organism. In other words, the likely potential receiving environment of an LMO encompasses both the environments where the LMO will be intentionally introduced as well as other environments which are likely to be exposed to the LMO.

To determine the likely potential receiving environment, risk assessors may consider potential pathways for dispersal of the LMO as well as the habitats where the recipient/parent organism(s) may persist or proliferate. As such, during a risk assessment, in addition to the area where the LMO will be intentionally introduced, the relevant characteristics of the likely potential receiving environment of an LMO should also be thoroughly examined with particular attention given to areas where exposure levels to the LMO will be the highest.

The characterization of the likely potential receiving environment takes into account its ecological characteristics, including physical location/geography, climate, its biological entities and their interactions. The characterization of the likely potential receiving environment will help in selecting appropriate assessment endpoints for the risk assessment (see Module 2) and will also affect the assessment of the potential interactions of the LMO with other organisms.

Information about the likely potential receiving environment can include considerations on both large scale (e.g. climate) and small scale characteristics (e.g. microclimate) depending on the complexity of the environment. The type of information on the likely potential receiving environment and the level of detail depend on the nature of the LMO and its intended use, in accordance with the case-by-case principle.

Below are descriptions of some physical and biological characteristics of the likely potential receiving environment(s) that can be considered in the risk assessment of LMOs. This is an indicative list thus the information required to satisfy the needs of the assessment will vary depending on the nature of the LMO and its intended use.

[note: the location of the text highlighted in gray was changed slightly in relation to the original document for a better alignment]

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
Likely potential receiving environment(s) – *physical characteristics* The physical or "abiotic" characteristics of the likely potential receiving environment may have a great impact on the ability of an LMO to survive and persist. *Geography and climate* – Geography encompasses characteristics such as latitude, which will influence day-length, and altitude. Climate encompasses temperature, precipitation, humidity, wind and other meteorological measures over long periods of time. For the purposes of environmental risk assessment, geography and climate are among the most important factors impacting the ability of an LMO to survive and persist. For LM plants, temperature and precipitation are likely to be key determinants. Seasonality (variations in climate on an annual cycle) can also be an important consideration in the potential survival and persistence of an LMO. *Soil* – The type and quality of soil can greatly influence the ability of an LM plant to survive or persist without land management. The type and quality of a soil are heavily influenced by the organisms living in its proximity, but abiotic factors such as climate, geography and topography will also all play a role in determining its characteristics (e.g. mineral content, moisture level, texture etc.). *Management status* – The management status of an environment is a measure of how much human intervention takes place in order to maintain a particular condition. A separate but related concept is "disturbance" which can be considered the amount of human activity that affects the environment but without the intention of maintaining a particular condition. Management and disturbance may greatly influence the ability of an LMO to survive and persist in the environment. Likely potential receiving environments can range from highly managed to unmanaged and from highly disturbed to undisturbed.	

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
Likely potential receiving environment(s) – *biological characteristics* The biological characteristics of the likely potential receiving environment consist of all the living organisms present in the environment, its biological communities and the interactions among them. Both managed and unmanaged environments contain complex biological characteristics that pose challenges for environmental risk assessments. As with any other organism, an LMO released into the environment is expected to have many interactions with other organisms. For the purposes of environmental risk assessment, it is critical to develop verifiable risk scenarios and identify the appropriate species that may be impacted by the presence of the LMO in the environment. For example, gene flow and possibly introgression may occur when sexually compatible species are present in the likely potential receiving environment. The selection of suitable representative species in the likely potential receiving environment is also informative (see section on "Selecting relevant assessment endpoints or representative species"). As seen above, an analysis of possible dispersal routes and mechanisms is important when establishing the likely potential receiving environments. Different dispersal mechanisms may exist and could be inherent either to the LMO (e.g. altered seed characteristics), its intended use (e.g. shipment practices) or the receiving environment (e.g. proximity to a river). A scientifically sound risk assessment takes into consideration all possible dispersal mechanisms, keeping in mind the biology of the LMO and non-modified recipient or parental organism(s), in a concerted manner for each case. It may not be possible or practical to consider every possible interaction between the LMO and the receiving environment. Such challenges and limitations should be acknowledged during the risk assessment process.	

[note: the location of the text highlighted in gray was changed slightly in relation to the original document for a better alignment]

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects

Intended use

The characteristics of the intended use of an LMO and management practices associated with it, such as tilling and the use of pesticides, can provide valuable information and context for the risk assessment process. Understanding the intended use also helps a risk assessor to perform an exposure assessment starting with the environment where the LMO will be deliberately introduced followed by considering whether or not the LMO is likely to disseminate or persist outside of this environment.

To illustrate how the intended use can affect the likelihood of a risk posed by an LMO, a hypothetical case of an LM tree being used for wood production could be considered, in which the first flowering would occur after 15 years of planting, but logging would take place after only 10 years. As such, the intended use would result in the LM tree being logged before its first flowering. Consequently, in this hypothetical case, the intended use would influence the likelihood of potential outcrossing[(10)] of this LM tree.

Information regarding the intended use of the LMO may also take into account any new or changed use in comparison to the recipient or parental organism(s), for example, in cases where the recipient or parental organism(s) is a crop for human consumption but the intended use of the LMO is the production of a compound for pharmaceutical or industrial use.

The scale and type of the introduction into the environment, for example, field trials versus commercial releases, and whether or not any risk management strategy is being proposed, may also be relevant when considering the intended use. Many regulatory frameworks, for instance, require that submissions for field trials be accompanied by information on risk management strategies to reduce exposure to the LMO.

Considerations on the intended use may also take into account national and regional experiences with similar organisms, their management and exposure to the environment.

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
	Points to consider regarding the intended use and the likely potential receiving environment: (a) Protection goals and assessment endpoints relevant to the likely potential receiving environment (see "Planning phase of the risk assessment", "Establishing the context and scope"); (b) Availability of sufficient data to establish a meaningful *baseline* for the likely receiving environment which will serve as a basis for the risk assessment; (c) The intended spatial scale, duration and level of confinement (such as biological confinement) of the environmental release, taking into account user practices and habits; (d) Characteristics of the likely potential receiving environment including relevant ecosystem functions and services, in particular its attributes that are relevant to potential interactions of the LMO that could lead to adverse effects (see also paragraph (k) below),* taking into account the characteristics of the components of biological diversity, particularly in centres of origin and centres of genetic diversity; (e) Potential adverse effects concerning target organisms such as pests developing resistance to the target trait and weeds developing resistance to the herbicide. * Examples of relevant attributes of the receiving environment include, among others: (i) ecosystem type (e.g., agroecosystem, horticultural or forest ecosystems, soil or aquatic ecosystems, urban or rural environments); (ii) extension of dimension (small, medium, large or mixed scale); (iii) previous use/history (intensive or extensive use for agronomic purposes, natural ecosystem, or no prior managed use in the ecosystem); (iv) the geographical zone(s) in which the release is intended, including climatic and geographic conditions and the properties of soil, water and/or sediment; (v) specific characteristics of the prevailing faunal, floral and microbial communities including information on sexually compatible wild or cultivated species; and (vi) biodiversity status, including the status as centre of origin and diversity of the recipient organism and the occurrence of rare, endangered, protected species and/or species of cultural value.

Step 1: Identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects	
	Points to consider regarding the potential adverse effects resulting from the interaction between the LMO and the likely potential receiving environment: (a) Characteristics of the LMO in relation to the likely potential receiving environment (e.g., information on phenotypic traits that are relevant for its survival, or its potential adverse effects – see also paragraph (e) above); (b) Considerations for *unmanaged and managed ecosystems*, concerning the use of an LMO, that are relevant for the likely potential receiving environment. These include potential adverse effects resulting from the use of an LMO, such as changes in farm management practices; dispersal of the LMO through mechanisms such as seed dispersal or *outcrossing* within or between species, or through transfer into habitats where the LMO may persist or proliferate; as well as effects on species distribution, food webs and changes in bio-geochemical characteristics; (c) Potential for outcrossing and transfer of *transgenes*, via *vertical gene transfer*, from an LMO to other sexually compatible species that could lead to *introgression* of the transgene(s) into populations of sexually compatible species, and whether these would lead to adverse effects; (d) Whether *horizontal gene transfer* of transgenic sequences from the LMO to other organisms in the likely potential receiving environment could occur and whether this would result in potential adverse effects. With regard to horizontal gene transfer to micro-organisms (including viruses), particular attention may be given to cases where the LMO is also a micro-organism; (e) Potential adverse effects on non-target organisms such as toxicity, allergenicity and *multi-trophic effects* which can affect the survival, development, or behaviour of these organisms; (f) Potential adverse effects of the incidental exposure of humans to (parts of) the LMO (e.g., exposure to modified gene products in pollen), and the toxic or allergenic effects that may ensue taking into account the agricultural practices that may be used with the LMO, such as type of irrigation, number and amount of herbicide applications, methods for harvesting and waste disposal, etc; (g) *Cumulative effects* with any other LMO present in the environment.

Step 2: Evaluation of the likelihood	
This step entails an evaluation of the likelihood, i.e. probability, of the adverse effect occurring, taking into account the level and kind of exposure of the likely potential receiving environment to the LMO. After the potential adverse effects of the LMO have been identified, the risk assessment proceeds to a formal analysis of the likelihood and consequence of these effects with respect to the identified assessment endpoints. Although the steps of evaluating likelihood and consequences are dealt with separately in Annex III of the Protocol, some risk assessment approaches consider these steps simultaneously or in reverse order. The likelihood of an adverse effect is dependent upon the probability of one or a series of circumstances actually occurring. It is difficult to describe in detail an evaluation of likelihood or consequence without using an example because the evaluation is dependent on the nature of the LMO, the receiving environment and, if appropriate, on the risk scenario used. The following slide contains some examples.	To determine and characterize the overall risk of an LMO (step 4), risk assessors evaluate the likelihood that each of the potential adverse effects identified in step 1 will occur. The evaluation of likelihood may be undertaken at the same time as the evaluation of the consequences should the adverse effects be realized (step 3) or in an inverse order. This step may be referred to as “exposure assessment” where plausible pathways of a hazard leading to adverse effects are identified. It aims to determine whether the receiving environment will be exposed to an LMO that has the potential to cause adverse effects, taking into consideration the intended transfer, handling and use of the LMO, and the expression level, dose and environmental fate of transgene products For each of the risk hypotheses or scenarios identified in step 1, the route of exposure to the LMO being assessed (or its products) should be determined. Furthermore, when possible the causal link between the LMO and the potential adverse effect should be established. This can be achieved by building conceptual models describing relationships between the LMO, pathways of exposure and potential adverse effects in the environment, taking also into account risks to human health. For example, for an LMO producing a potentially toxic gene product, oral, respiratory or dermal exposure pathways could be relevant. Experimental studies and models may be used for an assessment of the potential level and type of exposure, combined with the use of statistical tools relevant for each case. Past experience with similar situations (e.g., same recipient organism, LMO, trait, receiving environment, etc), if available, may also be used in assessing the level and type of exposure, taking into account user practices and habits. In some circumstances, particularly when there is a high level of uncertainty in assessing the likelihood, it may be difficult to assess the likelihood of adverse effects being realized. In such cases, it may be useful to assign a likelihood of 100% that an adverse effect will occur and concentrating on the evaluation of its consequences. Likelihood may be expressed quantitatively or qualitatively. For example, qualitative terms could include ‘highly likely’, ‘likely’, ‘unlikely’, and ‘highly unlikely’. Parties may consider describing these terms and their uses in risk assessment guidelines published or adopted by them.

Step 2: Evaluation of the likelihood	
In a case where outcrossing of the transgene with a non-modified organism is determined to be possible (i.e. the two species are sexually compatible), the risk assessment may consider both the likelihood of the outcrossing and, if relevant, the likelihood of the LMO progeny to persist or proliferate. Considerations on the latter may be based, for example, on assessing whether or not the transgene would affect the fitness level of the progeny (i.e. the capability of individuals to compete and reproduce in a given environment). If the transgene induces a positive fitness effect, the likelihood that the population resulting from the outcrossing would increase is high. On the other hand, transgenes that have a negative fitness effect would result in a low likelihood that the resulting population would increase. Transgenes that have a neutral impact on fitness may persist in populations at low levels depending on the rate of outcrossing or introgression as well as the overall population dynamics of the species. ***EXAMPLE: Likelihood of introgression***	(a) Factors that may affect spread of the LMO, such as its ecological range and ability to move; its reproductive ability (e.g., numbers of offspring, time to set seed, abundance of seed and vegetative propagules, dormancy, pollen viability); and its ability to spread using natural means (e.g., wind, water) or anthropogenic mechanisms (e.g., rearing or cultivation practices, seed saving and exchange, etc); (b) Factors that affect presence or persistence of the LMO that may lead to its establishment in the environment, such as, in the case of LM plants, lifespan, seed dormancy, ability of LM seedlings to establish among existing wild or cultivated vegetation and to reach reproductive stage, or the ability to propagate vegetatively; (c) When assessing the likelihood of outcrossing from the LMO to sexually compatible species, the following issues are relevant: (i) The biology of the sexually compatible species; (ii) The potential environment where the sexually compatible species may be located; (iii) Persistence of the LMO in the environment; (iv) Introgression of the transgene into the sexually compatible species;

Step 2: Evaluation of the likelihood	
In a case where the risk scenario involves the potential toxicity of an LM plant (or a substance produced by an LM plant) to a herbivorous insect: the analysis of likelihood may consider the probability that the insect will be present, that the insect will feed on the LMO and that the insect will ingest a sufficient quantity of the LMO to suffer an adverse effect. In evaluating the likelihood of adverse effects occurring, one may consider probabilities on an individual level (e.g. what are the chances an individual insect may consume the LM plant) or on a population level (e.g. what percentage of the population of insects will come into contact with the LMO) or both.	(d) The relevant characteristics of the likely potential receiving environment that may be a factor in the occurrence of the potential adverse effects (see also step 1 (f), (g) and (i)), taking into account the variability of the environmental conditions and long-term adverse effects related to the exposure to the LMO; (e) Levels of expression in the LMO and persistence and accumulation in the environment (e.g., in the food chain) of substances with potentially adverse effects newly produced by the LMO, such as toxins, allergens and some insecticidal proteins. In the case of field trials, the level of persistence and accumulation in the receiving environment may be low depending on the scale and temporary nature of the release, and the implementation of management measures; (f) Information on the location of the release and the receiving environment (such as geographic and biogeographic information, including, as appropriate, geographic coordinates); (g) Persistence of the transgene in the ecosystem; and (h) Expected type and level of exposure in the environment where the LMO is released, and mechanisms by which incidental exposure could occur at that location or elsewhere (e.g., *gene flow*, incidental exposure due to losses during transport and handling, intentional spread by people, or unintentional spread by people via machinery, mixed produce or other means).

Step 3: Evaluation of the consequences	
The consequence of an adverse effect is the outcome, extent and severity of an adverse effect associated with exposure to an LMO, its handling and use, or its products (in the context of Annex III paragraph 5). Should adverse effects occur, they may be severe, minimal, or anywhere in between. The evaluation of the consequences may consider the effects on individuals (e.g. mortality, reduced or enhanced fitness, etc.) or on populations (e.g. increase or decrease in number, change in demographics, etc.) depending on the adverse effect under evaluation. The risk assessment should consider the consequences of each adverse effect based on a concerted analysis of what is known about the LMO, the likely potential receiving environment and the assessment endpoints, as well as the likelihood assessment. ***EXAMPLE: Consequences of effects to non-target organisms***	This step, which may also be referred to as "hazard characterization", describes an evaluation of the magnitude of the consequences of the possible adverse effects, based on the risk scenarios established in step 1, paying special attention to protected areas and centres of origin and centres of genetic diversity, and taking into account protection goals and endpoints of the country where the environmental release may take place. As discussed in the previous step, the evaluation of consequences of adverse effects may be undertaken at the same time as the evaluation of likelihood (step 2) or in an inverse order. In this step, results of tests conducted under different conditions, such as laboratory experiments or experimental releases, may be considered. The scale and duration of the intended use (e.g., small or large) may influence the severity of potential consequences and should therefore be taken into account. The evaluation of consequences of adverse effects should be considered in the context of the adverse effects caused by the non-modified recipients or parental organisms in the likely potential receiving environment (see Planning Phase of the Risk Assessment). The evaluation of consequences may also consider the adverse effects associated with the existing practices or with practices that will be introduced along with the LMO (such as various agronomic practices, for example, for pest or weed management). It is important to also assess in this step the duration of the potential adverse effect (i.e., short or long term), the scale (i.e., are implications local, national or regional), the mechanisms of effect (direct or indirect), the reversibility (or lack thereof) of effects, and the expected ecological scale (i.e., individual organisms – for example of a protected species – or populations). The evaluation of the consequence of adverse effects may be expressed qualitatively or quantitatively. For instance, qualitative terms such as 'major', 'intermediate', 'minor' or 'marginal' may be used. Parties may consider describing these terms and their uses in risk assessment guidelines published or adopted by them.

Step 3: Evaluation of the consequences	
Also using an example where gene flow and introgression could lead to a potential adverse effect, what impact the presence of a transgene will have on biodiversity will depend on its effect on individual fitness as well as on the importance of that species relative to the protection goals. For instance, if a sexually compatible species, present in the receiving environment, is directly relevant to a biodiversity protection goal (e.g. it is a protected species) then the impact on biodiversity can be assessed by looking directly at the impact of the transgene on the population. If the sexually compatible species is not directly related to a biodiversity management goal, then the impact of the expression of the transgene will be dependent on indirect interactions. Indirect effects may be challenging to assess (see step 1), and are dependent on the ecological importance of the species.	*Points to consider:* (a) Relevant knowledge and experience with the non-modified recipient or parental organisms, or current use of the organism, in the likely potential receiving environment, and their interactions with other species, including sexually compatible species. This may include the effects of: (i) Agricultural practices on the level of inter- and intra-species gene flow; dissemination of the recipient organism; abundance of volunteers in crop rotation; change in abundance of pests, beneficial organisms such as pollinators, decomposers, organisms involved in biological control or soil microorganisms involved in nutrient cycling; (ii) Pest management affecting non-target organisms through pesticide applications or other management approaches while following accepted agronomic practices; (iii) The behaviour of populations of other species, including interactions between predators and prey, their role in food webs and other ecological functions, disease transmission, allergies and interaction with humans or other species; (b) Consequences resulting from combinatorial and cumulative effects in the likely potential receiving environment;[2] (c) Relevant knowledge and experience with the LMO in similar receiving environments; (d) Results from laboratory experiments examining, as appropriate, dose-response relationships or particular effect levels (e.g., *EC50*, *LD50*, *NOEL*) for acute, chronic or sub-chronic effects including immunogenic effects; (e) Results from field trials evaluating, for instance, potential invasiveness; and (f) Possible consequences of transgene introgression resulting from outcrossing/interbreeding to sexually compatible species.

[2] See "Use of terms" section.

Step 4: Estimation of the overall risk	
This step consists of the integration of the likelihood and consequence of each of the individual risks identified through the preceding steps and takes into account any relevant uncertainty that emerged thus far during the process. In some risk assessment approaches, this step is referred to as "risk characterization". To date, there is no universally accepted method to estimate the overall risk but a variety of guidance materials are available that address this topic (see for instance, documents under "Scientific and technical issues / risk assessment" in the Biosafety Information Resource Centre, BIRC).	The purpose of this step, which may also be referred to as "risk characterization", is to determine and characterize the overall risk of the LMO. This can be achieved by characterising and analysing individual risks on the basis of an analysis of the potential adverse effects completed in step 1, their likelihood (step 2) and consequences (step 3), and combining them into an estimation of the overall risk, taking into consideration any relevant uncertainty that was identified in each of the preceding steps and how it could affect the estimation of the overall risk of the LMO (see "Identification and consideration of uncertainty" under "Overarching issues in the risk assessment process" above). To date, there is no universally accepted approach for estimating the overall risk but rather a number of approaches are available for this purpose. For example, the characterization of the overall risk often derives a best estimate of risk from multiple lines of evidence. These lines of evidence may be quantitatively or qualitatively weighted and combined. Risk matrixes, risk indices or models may be used for this purpose. * * See references in the list of background materials.

Step 4: Estimation of the overall risk	
In rare instances, the risk characterization results in a quantitative value (e.g. 6% of a population will be exposed to a stressor, and of that percentage half will experience mortality). More frequently, the risk characterization for an LMO will be qualitative. In such cases, description of the risk characterization may be expressed as, for instance, 'high', 'medium', 'low', 'negligible' or 'indeterminate due to uncertainty or lack of knowledge'. The outcome of this step is the assessment of the overall risk of the LMO. Once this is achieved, it is helpful to determine, as an internal quality control, whether the risk assessment has met the criteria established at the beginning of the process taking into account also those criteria established in the relevant policies in practice with regard to the protection goals, assessment endpoints and risk thresholds (i.e. the level of tolerance to a certain risk or the level of change in a particular variable beyond which a risk is considered unacceptable). ***FIGURE – Estimation of overall risk*** ***FIGURE – Classification of risk***	A description of the risk characterization may be expressed qualitatively or quantitatively. Qualitative terms such as 'high', 'medium', 'low', 'negligible' or 'indeterminate' (e.g., due to uncertainty or lack of knowledge) have been used to characterize the overall risk of an LMO. Parties could consider describing these terms and their uses in risk assessment guidelines published or adopted by them. The outcome of this step should include a description explaining how the estimation of the overall risk was performed.

Step 5: Acceptability of risk and identification of risk management and monitoring strategies	
Annex III of the Protocol states that the risk assessment methodology may entail "a recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage these risks" and "where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment".3 The following slides deal with the identification of risk management and monitoring strategies. Issues related to the acceptability of risks are under "Preparing a risk assessment report and recommendation".	In step 5, risk assessors prepare a report summarizing the risk assessment process, identified individual risks and the estimated overall risk, and provide recommendation(s) as to whether or not the risks are acceptable or manageable and, if needed, recommendation(s) for risk management options that could be implemented to manage the risks associated with the LMO. The recommendation is made in the context of criteria for the acceptability of risk that were identified in the planning phase of the risk assessment, taking into account established protection goals, assessment endpoints and risk thresholds, as well as risks posed by the non-modified recipient organism and its use. This step is an interface between the process of risk assessment and the process of decision-making. Importantly, while the risk assessor provides a recommendation as to whether or not the risks are acceptable or manageable, the ultimate decision about whether or not to approve the LMO notification is a prerogative of the decision maker. Moreover, the "acceptability" of risks is typically decided at a policy level and may vary from country to country.

3 Paragraphs 8(e) and (f) of Annex III.

Step 5: Acceptability of risk and identification of risk management and monitoring strategies

Risk management

Risk management strategies refer to measures to ensure that risks identified in the risk assessment are reduced or controlled which may be implemented after the LMO is introduced into the environment (or placed in the market, if applicable). Risk management strategies can be useful to increase confidence when dealing with uncertainty or, in the case where risks have been identified, to reduce the likelihood or impact of the potential adverse effect.

Risk management strategies may aim to reduce the likelihood or consequences of potential adverse effects and are referred to as "preventive measures" and "mitigation measures", respectively. Some approaches to risk assessment may also include the identification of measures to control an adverse effect should it occur.

For LMOs, common risk management strategies have typically been designed to reduce the likelihood of exposure, but depending on the specific case, management options might include a variety of measures that are directly or indirectly related to the LMO. Some examples of risk management strategies for LMOs include: minimum distances from sexually compatible species if there is evidence that gene flow could cause adverse effects, destruction of seeds remaining in the field or of volunteers after harvest, restrictions from introduction into specified receiving environments, etc.

Certain risk assessment steps, particularly the evaluation of likelihood and consequences may need to be re-evaluated to take into account each of the identified risk management strategies since these may affect the estimation of the overall risks.

EXAMPLE: Application of management strategies for risks from the deliberate release or marketing of LMO(s)

Points to consider related to the risk management strategies:

(a) Existing management practices, if applicable, that are in use for the non-modified recipient organism or for other organisms that require comparable risk management and that might be appropriate for the LMO being assessed (e.g., physical containment, isolation distances to reduce outcrossing potential of the LMO, modifications in herbicide or pesticide management, crop rotation, soil tillage);

(b) Methods to detect and identify the LMO, and their specificity, sensitivity and reliability in the context of environmental monitoring (e.g., monitoring for short- and long-term, immediate and delayed effects; specific monitoring on the basis of scientific hypotheses and supposed cause/effect relationship as well as general monitoring), including plans for appropriate contingency measures to be applied if warranted based on monitoring results;

(c) Management options and their feasibility in the context of the intended and expected use (e.g., isolation distances to prevent outcrossing, and the use of refuge areas to minimize the development of resistance to insecticidal proteins); and

(d) Methods for evaluating the proposed risk management and monitoring strategies for feasibility, efficacy and effectiveness.

Step 5: Acceptability of risk and identification of risk management and monitoring strategies

Monitoring

A risk assessor may identify the need for a strategy to monitor the receiving environment for adverse effects that may arise after the introduction of the LMO and include it as part of the recommendations for the Competent National Authority(ies). This may happen, for instance, when the level of uncertainty could affect the overall conclusions of the risk assessment. Moreover, some biosafety frameworks may have a policy to request a plan for monitoring as part of the risk assessment of all or particular types of LMOs.

Monitoring after the release of the LMO aims at detecting changes (e.g. in the receiving environment(s) or in the LMO) that could lead to adverse effects.

Monitoring strategies may be designed on the basis of the protection goals identified by national legislation and regulation, if available, and parameters that are relevant to the indication of any increasing risk to the assessment endpoints in a "top-down" approach, or on the basis of specific risks in a "bottom-up" approach.

The strategies may include "general surveillance" that can make use of existing, broader monitoring programs that may identify unexpected effects of the LMOs or traits, such as long-term effects; or be "case-specific" where potential adverse effects identified during the risk assessment are investigated. Monitoring for the development of resistance in insect pests following introduction of pesticide producing LM crops would be an example of a "case-specific" scenario. Monitoring for the abundance of beneficial insect species in an environment would be an example of "general surveillance".

Where it is appropriate, other potential adverse effects such as delayed, cumulative, combinatorial or indirect effects resulting from the LMO, the trait or the inserted or modified genes may be considered in the post-release monitoring strategies.

The level of specificity of the monitoring strategies may vary depending on the LMO(s), the intended use(s) and/or the likely potential receiving environment(s). Therefore, it is essential that a detailed methodology for each identified strategy also be identified. The methodology may include, for example, the frequency, locations and methods of sampling, as well as methods of analysis (e.g. laboratory testing).

EXAMPLE: Post-market monitoring

EXAMPLE: Case-specific monitoring and general surveillance of LM plants

Step 5: Acceptability of risk and identification of risk management and monitoring strategies	
	In evaluating the acceptability of the overall risk of the LMO, it is important to consider whether risk management options can be identified that could address identified individual risks and the estimated overall risk as well as uncertainties. The need, feasibility and efficacy of the management options, including the capacity to enact them, should be considered on a case-by-case basis. If such measures are identified, the preceding steps of the risk assessment may need to be revisited in order to evaluate how the application of the proposed risk management measures would change the outcome of the steps. The recommendation on the acceptability of risk(s) should take into account any available scientific analysis of potential benefits for the environment, biodiversity, and human health (e.g., change in the use of crop protection products, reduction of infections in the case of mosquitoes), and should also take into account risks associated with other existing user practices and habits. Further, the sources and nature of uncertainty that could not be addressed during the preceding steps of the risk assessment should be described in relation to how they could affect the conclusions of the risk assessment. For assessments where uncertainties could not be addressed, difficulties encountered during the risk assessment should be made transparent to the decision makers. In such cases, it may also be useful to provide an analysis of alternative options to assist the decision makers.

Step 5: Acceptability of risk and identification of risk management and monitoring strategies	
	In accordance with Annex III paragraph 8(f) "where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment". Monitoring can be a means to reduce uncertainty, to address assumptions made during the risk assessment, to validate conclusions of the assessment on a wider (e.g., commercial) level of application, and to establish a causal link or pathway between LMOs and adverse effects. Monitoring may also be used to evaluate whether risk management strategies are being implemented effectively, including whether those strategies are able to detect potential adverse effects before the consequences are realized. Monitoring can also be applied as a tool to detect effects that were not anticipated in the risk assessment and long-term adverse effects. The issues mentioned in the section 'Establishing the context and scope' may be taken into consideration again at the end of the risk assessment process to evaluate whether the objectives that were set out at the beginning of the risk assessment have been met. The recommendation(s) are submitted, typically as part of a risk assessment report, for consideration in the decision-making process. *Points to consider related to the acceptability of risks:* (a) Established criteria and thresholds for determining risk acceptability, including those set out in national legislation or guidelines; (b) Protection goals and assessment endpoints as identified when establishing the context and scope for a risk assessment; (c) Any relevant experience with the non-modified recipient organism(s) or other reference line(s) (including practices associated with their use in the likely potential receiving environment) which were used to establish the baseline for the risk assessment; (d) Scientific benefit analyses, carried out using similar principles of sound science as those used throughout the risk assessment; (e) Ability to identify, evaluate, manage and confine adverse effects in the event that the LMO is released into the environment, as well as to take appropriate response measures.

Preparing a risk assessment report and recommendation

The risk assessment report

The outcomes of a risk assessment are often presented in the form of a written report prepared by the risk assessor(s). The report is primarily intended to assist the decision makers in making informed decisions regarding the safe use of an LMO.

Presenting the results of a risk assessment could be categorized as a form of risk communication. As in any form of communication, risk assessors should be mindful of the intended recipients, which in addition to decision makers may also include regulators, risk managers, other risk assessors and the general public amongst others.

It is important that the report is presented in a well-structured form, which not only facilitates the deliberations of decision makers, but also allows for an easier exchange of information and experience. The context and scope of the risk assessment should be clearly explained as other institutions (e.g. in the same or in different countries) may have an interest in understanding how the risk of a particular LMO was assessed.

With regard to the sharing of information, a Party to the Protocol is required to submit to the Biosafety-Clearing House (BCH) all "summaries of its risk assessments or environmental reviews of living modified organisms generated by its regulatory process, and carried out in accordance with Article 15, including, where appropriate, relevant information regarding 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" (Article 20). This will include all risk assessments generated to support decisions regarding LMOs for intentional introduction into the environment (Articles 8, 10 and 13) or for direct use as food or feed, or for processing (Article 11) whether they are triggered by a transboundary movement or by an internal request.

The required contents and format of a risk assessment report are generally defined by the Competent National Authority(ies) that have the responsibility to make decisions on the LMO(s) in the context of the national biosafety framework.

EXAMPLE: Risk communication

The risk assessment report

A risk assessment report typically comprises of an analytic synthesis of all the relevant steps and results of the risk assessment process, including an overview of the context and scope of the risk assessment, methodology used and a detailed summary of the results of the overall risk estimation, including the identification of individual risks, as well as the likelihood and consequences of the potential adverse effects.

The report may also contain an evaluation of the availability and quality of the scientific and technical information that was deemed necessary to perform the assessment and characterize the risks, and whether or not there were gaps in the information.

An analysis of all identifiable uncertainties and how they may impact the overall conclusions of the assessment is also a critical element of the report. This includes uncertainties identified at each step of the risk assessment process as well as those remaining at the end of the risk assessment,

Finally, the risk assessment report often contains a set of recommendations regarding the acceptability and manageability of the risks posed by the LMO and the identification of appropriate risk management and monitoring strategies.

The information above can be organized under five broad topics depending on the requirements of the National Authority that is responsible for the risk assessment:

(a) Background, context and scope of the risk assessment;
(b) Characterization and estimation of risks;
(c) Description of risk management and monitoring strategies identified during the risk assessment;
(d) Consideration of remaining uncertainty; and
(e) Recommendations as to whether or not the risks are acceptable or manageable.

An overview of the information which may be included under each of these topics may be found in the following sections.

The risk assessment report	
Background, context and scope of the risk assessment This part of the report focuses on describing the issues that were considered while setting the context and scope of the risk assessment. Basically, this section of the report sets the scene for the reader to follow a clear progression through the subsequent sections of the report. A risk assessment report usually specifies the mandate that was given to the risk assessor(s) and includes a description of the procedure that was followed in conducting the risk assessment, an indication of which institution has carried out the risk assessment, and which, if any, other institutions were consulted or were part of the process. Any other information that helps in understanding the context in which the risk assessment was carried out is also typically included in this part of the report. Previous approvals or prohibitions of the same LMO, if any, including the regulatory status of the LMO in the country of export or import as well as in any other country may also be included in this section, if appropriate. The report describes how the requirements of the national regulatory framework were taken into account including which protection goals were identified as relevant in the context of the risk assessment and how assessment endpoints were selected.	

The risk assessment report	
Background, context and scope of the risk assessment The following information may be included in this section of the report: • Contact details of the LMO developer; • Type of approval sought (e.g. introduction into the environment); • Contact details of the institution responsible for the risk assessment; • Relevant regulation; • Relevant protection goals and assessment endpoints; • Previous approvals or prohibitions of the same LMO; • Overview of the terms of reference for the risk assessment; and • Consulted experts or panel of experts, if applicable, and how the involved experts were chosen and how possible conflict of interests were identified and was managed. In some cases, the bulk of information presented in this section of the report may be extracted from the request triggering the risk assessment, the national regulatory framework, including environmental and biosafety policies or guidelines, and national biosafety-related databases.	

The risk assessment report	
Characterization and estimation of risks This section of the report focuses on the outcomes of the risk assessment steps in accordance with the steps in Annex III of the Protocol and as described above. Depending on the specific mandate and scope of the risk assessment, the following information may be included in this section of the report: (a) Description of the LMO (e.g. recipient or parental organism(s), transformation method, inserted or modified sequences, novel traits, purpose of the genetic modification), its intended use and the likely potential receiving environment(s), including considerations on how the baselines were established and appropriate comparator(s) chosen; (b) Considerations of the availability and quality of information used during the risk assessment; (c) Methodology used in the risk assessment, explaining, if necessary, the use of terms; (d) Description of the potential adverse effects and risk scenarios arising from the novel characteristics of the LMO; (e) Analyses of the likelihood and consequences of each identified potential adverse effect; and (f) Estimation of the overall risk posed by the LMO. The information relevant to each of the items above may vary in nature and level of detail on case-by-case basis, depending on the LMO concerned, its intended use and the likely potential receiving environment. While information related to the description of the LMO and its intended use may be obtained in part from the LMO application, the bulk of information to be presented in this section of the report is obtained through the risk assessment process for the specific case at hand.	

The risk assessment report	
Description of risk management and monitoring strategies If risk management and monitoring strategies were identified during the risk assessment process (see step 5), the risk assessment report should contain a section detailing any strategies to minimize the risks identified. The risk assessment report may include, for instance: (a) How each identified strategy is expected to contribute to minimizing the likelihood or consequence of potential adverse effects (e.g. by reducing the exposure to the LMO or the consequences of the potential harm); (b) Details of the methodology for each identified risk management or monitoring strategy including, for instance, the frequency, locations and methods of sampling, as well as methods of analysis, including laboratory testing when appropriate; (c) Any uncertainty regarding the effectiveness of any such management or monitoring strategy; (d) An indication as to whether and how different management strategies can be combined to further minimize uncertainty or identified risks; and (e) Considerations on unintentional introduction into the environment and emergency measures as appropriate (see Article 17).	

The risk assessment report

Consideration of remaining uncertainty

As seen in the section on "Overarching issues", uncertainty is an inherent component of any risk assessment, and should be considered in a systematic manner at each step of the risk assessment process. Nevertheless, at the end of the risk assessment, uncertainties may still remain with regard to one or more specific steps in the process or about the likelihood or consequences of the potential adverse effects.

Annex III of the Protocol addresses this matter by requiring that "Where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment".[4]

Considerations of remaining uncertainties should be included in the risk assessment report. These considerations may include:

(a) Identification of major information gaps and, where appropriate, indication of whether gathering additional data (either before the release or after it by monitoring) would significantly increase the overall confidence in the results of the risk assessment;
(b) An analysis of uncertainty, including its types (e.g. gaps in the available information, limitations of the assessment methodology);
(c) Discussion on the level of scientific support to issues where there is uncertainty, including an analysis of different scientific views;
(d) Discussion of any assumption used in assessing the risks, including its strengths and weaknesses;
(e) Discussion of the potential for uncertainties to impact on the overall conclusions of the risk assessment; and
(f) Identification of any threats of serious or irreversible damage to the environment (basis for the adoption of the precautionary approach).

EXAMPLE: Uncertainty and an approach based on the precautionary principle

4 Paragraph 8(f) of Annex III.

The risk assessment report

Recommendation as to whether or not the risks are acceptable or manageable

Recommendations are one of the most important sections of a risk assessment report as they take into account the outcomes of the risk assessment to provide direct science-based advice to the intended recipients of the report. A recommendation as to whether or not the risks are acceptable or manageable should be kept within the scope of the risk assessment and based on its findings.

It is important to note that risk assessor(s) are requested to recommend whether the risks are “acceptable” or not. However, the definition of "acceptability" may not be part of a risk assessment but could be pre-established, for example, in thresholds included in government policies or in the mandate given to the risk assessor. Likewise, the final decision on whether to approve (with or without conditions) or prohibit the specific use of the LMO is taken during the decision-making process, which may take into account, depending of the national regulatory framework and among other things, government policies, public opinion, anticipated benefits, costs of the risk management measures and socio-economic considerations.

In addition to the issues mentioned above, the recommendations section of the report may also include any relevant information to be considered by the decision makers prior to making a decision. Some issues that may be relevant include:

(a) A recommendation as to whether or not one or more risk management or monitoring strategies should be implemented and, if so, the specific conditions for each such strategy;
(b) Considerations of remaining uncertainties; and
(c) A recommendation as to if and when the risk assessment should be re-visited.

The risk assessment process	
	FIGURE: The flowchart for risk assessment
