DRAFT ROADMAP FOR RISK ASSESSMENT

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This "roadmap" provides an overview of the process of conducting an LMO risk assessment in accordance with Annex III[1] to the Cartagena Protocol on Biosafety (the Protocol) and other all relevant articles. Annex III constitutes the basis of the Roadmap; as such, this Roadmap is a guidance document and does not replace Annex III. The Roadmap is aimed at enhancing the technical and scientific process of how to apply the steps within the process of risk assessment.

The purpose of this Roadmap is to provide a) further guidance on using Annex III with additional background material, b) a rationale for five key steps in the risk assessment, c) additional points to consider for each of the five steps, and e) direct access to useful references. This Roadmap may be useful as a reference for risk assessors when conducting new or reviewing existing risk assessments, and for developing capacity when a national risk assessment framework is not yet available.

The Roadmap applies to all types of LMOs and applications within the scope of the Protocol according to Annex III. However, it has been developed with a focus on LMO crop plants and living modified micro-organisms for environmental use, i.e. the types LMOs that have been used most extensively in environmental releases and for which there exists most experience with risk assessment:. The Roadmap is intended as a living document that will be shaped and improved on with time, as and when mandated by COPMOP, in the light of new experience, information and developments in the field of applications of LMOs,

INTRODUCTION

General introduction

Background

In accordance with the precautionary approach, 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, specifically focusing on transboundary movements[2].

For this purpose, Parties shall ensure that risk assessments are carried out when making informed decisions regarding living modified organisms (LMOs).

The objective of risk assessment is to *identify* and *evaluate* the potential adverse effects of LMOs on the conservation and sustainable use of biological diversity in the likely potential receiving environment, taking also into account risks to human health.[3]

According to the general priciples of Annex III of the Protocol, risk assessments shall be based, at a minimum, on information provided in accordance with Article 8 and other available scientific evidence in order to identify and evaluate the possible adverse effects of living modified organisms on the conservation and sustainable use of biological diversity, taking also into account risks to human health.[4]

[1] http://www.cbd.int/biosafety/articles.shtml?a=cpb-43
[2] http://www.cbd.int/biosafety/articles.shtml?a=cpb-01
[3] Annex III, 1
[4] Article 15, 1

According to the general principles of Annex III[5], risk assessment should be carried out in a scientifically sound and transparent manner, and can take into account expert advice of, and guidelines developed by, relevant international organizations. 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. Risks should be considered in the context of the risks posed by the non-modified recipients in the likely potential receiving environment. Risk assessment should be carried out on a case-by-case basis. The required information may vary in nature and level of detail from case to case, depending on the living modified organism concerned, its intended use and the likely potential receiving environment.'

The risk assessment process.

Risk assessment is a structured process. Paragraph 8 of Annex III provides a description of the key steps of the risk assessment process to identify, evaluate and manage potential risks, paragraph 9 describes points to consider in this process, depending on the case. The steps in paragraph 8 of Annex III describe an integrated process, whereby the results of one step may be relevant to other steps. Also, risk assessment is often conducted in an iterative manner, where certain steps may be repeated or reexamined, to increase the confidence in the conclusions in the risk assessment. Once a risk assessment has been concluded and new information arises that could change its conclusions, the risk assessment may need to be revisited, taking into account the newly available information at the relevant steps. Similarly, the issues mentioned in the 'Overarching issues' section below can be taken into consideration again at the end of the risk assessment process to determine whether the objectives and criteria set out at the beginning of the risk assessment have been met.

Risk assessment is done in a comparative manner, meaning that risks associated with LMOs should be considered in the context of the risks posed by the non-modified recipient or, as appropriate, with a non-modified organism of the same species, in the likely potential receiving environment. Experience with an LMO with the same, or, as appropriate, similar, genotypic and phenotypic characteristics may be considered in the risk assessment of an LMO. For instance, results from experimental trials or other environmental information and experience with the same LMO may be taken into account as information elements in a new risk assessment for that LMO. It is important, however, to check the validity of this information for the new risk assessment. For instance, it should be taken into account that the behaviour of a transgene in an LMO may depend very much on the genetic and biological background of the recipient, and on the ecological characteristics of the environment that the LMO is introduced into.

The concluding recommendations derived from the risk assessment in step 5 are but one of the considerations that are required to be taken into account in the decision-making process regarding the approval of an LMO. In other parts of the decision making process, other Articles of the Protocol or other relevant issues may also be taken into account. These Articles and some of the other issues are mentioned in the last paragraph of this Roadmap, entitled 'Related issues'.

Overarching issues in the design/planning phase of the risk assessment process

There are some overarching issues to consider in the design/planning phase of the risk assessment process to ensure the quality and relevance of information used. These entail, among others:

- Setting criteria for relevancy and requirement of data in the context of a risk assessment; data may be considered relevant if they can affect the outcome of the risk assessment.

- Establishment of scientifically robust standards for the inclusion of scientific information. *A link to a BCH page with additional guidance or supporting material will be provided.*
    - Data should be of an acceptable scientific quality. Data quality should be consistent with the accepted standard practices of scientific evidence gathering, and may include

[5] Annex III, 3 through 6

independent review of methods and design of the study. Data may be derived from a variety of sources, e.g. new experimental data, as well as data from the relevant scientific literature.

- The principles of transparency, verifiability and reproducibility (e.g. reporting of methods and data in sufficient detail), including accessibility (e.g. availability of further relevant and required data or information, or, if requested and as appropriate, of sample material, are of the most importance to ensure and verify that the risk assessment is carried out in a scientifically sound and transparent manner.

- Identification of the types and sources of uncertainty. *A link to a BCH page with additional guidance or supporting material will be provided.* Uncertainty can arise at each of the various steps of a risk assessment. To improve the overall risk estimation, an uncertainty analysis should be conducted in a consistent manner, at each step of the risk assessment. Types and sources of uncertainty can be, for instance, uncertainty in relation to available knowledge or information, or their interpretation; uncertainty inherent to technologies used, and uncertainty due to variability. Where there is uncertainty regarding the level of risk, this may be addressed by requesting further information on the specific issues of concern, by implementing appropriate risk management strategies and/or by targeted monitoring of the LMO in the receiving environment to address specific concerns. Remaining or lasting uncertainty, due to for instance lack of scientific data, ambiguity, or ignorance, may be addressed in decision making, by applying the Precautionary Approach, as stated in Article 1 of the Protocol. Alternatively, it may be addressed by recommending that a decision for approval, including management options as appropriate, may be considered after the deficient information has become available. Some types of uncertainties may be irreducible with the current state of knowledge.

Context and scoping of the risk assessment

In setting context and scope for a risk assessment, a number of aspects should be taken into consideration, as appropriate, that are specific to the Party involved and to the specific case of risk assessment. These aspects include, among others:

- The context and scope of risk assessment as laid down in existing policies and strategies, based on for instance regulations and international obligations of the Party involved as well as guidelines or regulatory frameworks that the Party has adopted; identification of protection goals, end-points and management strategies, derived from these policies and strategies. Consistency with these policies and strategies within the scope of the risk assessment may involve a process that includes risk assessors, decision-makers and various stakeholders prior to conducting the actual risk assessment.

- Framing the risk assessment process, taking into account the expected (potential) conditions of handling and use of the LMO, taking into account customary practices and habits, that could affect the protection goals or end-points; identification of relevant questions to be asked for that purpose.

- Identification of methodological and analytical requirements to achieve the objective of the risk assessment, as laid down for instance in guidance on risk assessment published or adopted by the Party involved, that must be complied with in risk assessment; including means of reviewing whether the risk assessment is in compliance with the methodology and requirements of the applicable guidance.

- The nature and level of details of the information required may depend on the intended use of the LMO, e.g. in a confined field experiment*[6], or an unconfined environmental release, such as commercial scale planting, and the likely potential receiving environment.

- Experience and history of use of the non-modified recipient, taking also into account its ecological function[7].

- Establishing criteria for describing the level of the (potential) adverseness of environmental effects of an LMO, as well as criteria for the terms that are used to describe the levels of likelihood (step 2 below), and the magnitudes of consequences (step 3, below) and risks (step 4) and the manageability of risks (step 5).

Links to BCH pages with guidance or other supporting material to these paragraphs will be provided.

THE RISK ASSESSMENT

To fulfill its objective under Annex III, as well as other relevant Articles of the Protocol, risk assessment is performed in five steps, as appropriate. For each step of the risk assessment process this Roadmap presents a rationale that explains the aim of the step as well as the points to consider. These points to consider are partly taken from paragraph 9 of Annex III; the points to consider in the risk assessment will depend on the case being analyzed. Some points to consider have been added, based on generally accepted methodology of LMO risk assessment and risk management.

Step 1: "An identification of any novel genotypic and phenotypic characteristics associated with the living modified organism that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health."[8]

Rationale: The purpose of this step is to identify biological changes resulting from the genetic modification that could change the interaction of the LMO with its environment in a way that could cause adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health. This step is similar to the 'hazard identification step' in other risk assessment guidance. The comparison of the LMO with the non-modified recipient or, as appropriate, with a non-modified organism of the same species, serves this purpose.

In this step plausible hazard scenarios are identified by which the identified novel, intended or unintended, genotypic and phenotypic, in summary, all relevant novel biological characteristics of the LMO may give rise to adverse effects in an interaction with the likely potential receiving environment. The points to consider provide information elements on which hazard identification can be built.

The type and level of detail of the information required in this step may vary from case to case depending on the nature of the modification of the LMO and on the scale of the intended use of the LMO.

Points to consider regarding the characterization of the LMO:

[6] Terms with an asterisk (*) do not apply to commercial releases, but may apply to confined or unconfined field trials.

[7] The term 'ecological function' (or: 'ecological services)' provided by an organism refers to the role of the organism in ecological processes. Which ecological functions or services are taken into account here will be dependent on the protection goals set for the risk assessment. For example organisms may be part of the decomposer network playing an important role in nutrient cycling in soils or be important as pollen source for pollinators and pollen feeders.

[8] The bold printed headings of each step are direct quotes from Annex III of the Protocol.

(a) Characteristics of the non-modified recipient (e.g. its biological characteristics, with particular attention to characteristics that, if changed, or interacting with other changed genes, could change the interaction of the non-modified recipient with the environment in a way that could cause adverse effects; its taxonomic relationships, its origin, centers of origin and centers of genetic diversity);

(b) Relevant characteristics of the genes that have been inserted into the LMO (e.g. functions of the gene product in the donor organism, with particular attention to characteristics that, when transferred to the recipient, could cause adverse effects);

(c) Molecular characteristics of the LMO related to the modification (e.g. transformation method, characteristics of the vector if and as far as it is present in the LMO, including its identity, source/origin and host range; characteristics of the insert(s), including gene products, expression level, function, its insertion site in the genome, stability or integrity) that are related to potential adverse effects. Availability and relevance of this information may vary according to the type of application, particularly at the stage of field releases*. Characteristics related to adverse effects may also result from altered expression levels of endogenous genes due to effects of a transgene (e.g. due to insertional disruption of a gene or to regulatory effects) and combinatorial/synergistic effects of the transgene product with endogenous genes or products of other transgenes present in the LMO.

(d) Identification of genotypic and phenotypic, biological changes in the LMO, either intended or unintended, in comparison with the non-modified recipient, considering those changes that could cause adverse effects;

Point to consider regarding the receiving environment:

(e) Characteristics of the likely potential receiving environment, in particular its attributes that are relevant to potential interactions of the LMO that could lead to adverse effects (see also paragraph (f));[9]

Points to consider regarding the potential adverse effects resulting from the interaction between the LMO and the receiving environment:

(f) Characteristics of the LMO in relation to the receiving environment (e.g. information on phenotypic traits that are relevant for its survival in or its interaction with the likely receiving environment; see also paragraph (e));

(g) Considerations for unmanaged and managed ecosystems (such as agricultural, forest and aquaculture systems) that are relevant for the likely potential receiving environment, including the potential for dispersal of the LMO through, for instance, seed dispersal or outcrossing within the species, in habitats where the LMO may persist or proliferate.

(h) Unintentional outcrossing and flow of transgenes from an LMO to other sexually compatible species may and occur. The consequences this process may include introgression of the transgene(s) into the population of the sexually compatible species. In such cases,

[9] Examples of relevant attributes of the receiving environment include, among others: (i) type (e.g. agroecosystem; horticultural or forest ecosystems, soil or aquatic ecosystems), (ii) structure (small, medium, large or mixed scale); (iii) previous use/history (intensive or extensive use for agronomic purposes, natural ecosystem, or no use of the ecosystem); (iv) the ecosystem type(s) or 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; (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.

considerations should include the biology of the sexually compatible species, effects of the transgene(s), if introgressed, in this genetic background, the potential environment where the sexually compatible species may be located, and possible adverse effects that may occur due to the presence of the transgenes in the sexually compatible species.

(i) Adverse effects as a consequence of horizontal gene transfer from the LMO, particularly if the LMO is a bacterium or a virus.

Links to BCH pages with guidance or supporting material for paragraphs of this step will be provided.

Step 2: "An evaluation of the likelihood of adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the living modified organism."

Rationale: The potential adverse effects identified in step 1 may result in risks, depending on the likelihood and the consequence of the effects. In order to determine, in step 4, the level of these risks, in this step 2 the likelihood of the adverse effects being realized has to be evaluated. One aspect of likelihood is whether the receiving environment will be exposed to the LMO in such a way that the identified adverse effects may actually occur, e.g. taking into consideration the intended use of the LMO, and the expression level, dose and environmental fate of transgene products. Other aspects that are usually taken into account here are the potential of the LMO, or its derivatives (i.e. sexually compatible organisms in which transgenes have introgressed), to spread and establish in the receiving environment, and whether that could result in the possibility to affect or displace other or related species, and the possibility of occurrence of adverse (e.g. toxic) effects on organisms (other than the 'target organism', if applicable, of the LMO). The levels of likelihood may be expressed as, for example, highly likely, likely, unlikely, highly unlikely, whereby it is recommended that the use of these terms has been described for instance in guidance on risk assessment published or adopted by the Party.

Points to consider:

(a) Information relating to the type and intended use, including proposed control measures if applicable, of the LMO as well as the scale of release;

(b) The relevant characteristics of the likely potential receiving environment that may experience or may be a factor in the occurrence of the potential adverse effects (see also Step 1, (e), (f) and (g));

(c) Levels of expression in the LMO and persistence and accumulation in the environment, e.g. in the food chain, of potentially harmful substances newly produced by the LMO, e.g. insecticidal proteins;

(d) Available information on the location of the release (in case of confined releases, e.g. maps[10] of release site*, biogeographical information), including information on the sexually compatible species, e.g. whether it is co-located with the LMO, and whether flowering occurs at the same time;

(e) Expected exposure to the environment and means by which incidental exposure could occur (e.g. gene flow, or incidental exposure due to losses during transport and handling).

Links to BCH pages with guidance or supporting material for paragraphs of this step will be provided.

Step 3: "An evaluation of the consequences should these adverse effects be realized."

[10] The term 'maps' may include more detailed geographic information, e.g. coordinates, as appropriate under the legislation of the Party involved.

Rationale: This step describes an evaluation of the severity of the consequences in the likely potential receiving environment, taking into account, among others, results of tests done under different conditions such as laboratory experiments or small scale field releases. The evaluation should be considered in the context of the adverse effects caused by the non-modified recipient or by a non-modified organism of the same species, or of the adverse effects that occur in the environment due to comparable existing practices. The evaluation of the consequence of adverse effects being realized may be expressed as, for instance, major, intermediate, minor or marginal, whereby it is recommended that the use of these terms has been described for instance in guidance on risk assessment published or adopted by the Party.

Points to consider:

(a) Relevant experience with consequences of existing practices with the non-modified recipient or with a non-modified organism of the same species in the likely potential receiving environment, as applicable, for establishing baselines (e.g. consequences from agricultural practices, such as the level of inter- and intra-species gene flow, dissemination of the recipient, abundance of volunteer plants in crop rotation; or from pest management, including effects on non-target organisms in pesticide applications while following accepted agronomic practices);

(b) Direct and indirect, immediate and delayed effects, as well as cumulative or combinatorial and synergistic effects leading to adverse consequences.

Links to BCH pages with guidance or supporting material for paragraphs of this step will be provided.

Step 4: "An estimation of the overall risk posed by the living modified organism based on the evaluation of the likelihood and consequences of the identified adverse effects being realized."

Rationale: The purpose of this step is to determine and characterize all identified risks posed to biological diversity taking also into account human health, based on the identified potential adverse effects (step 1), and estimating the cumulative level of risk by combing the assessments of their likelihood (step 2) and their consequences (step 3), taking into consideration any relevant uncertainties that emerged in the preceding steps. It should then be determined whether the identified risks meet the criteria for acceptability relative to assessment endpoints as established in relevant statutes or regulations. 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 (see also step 5). The estimation of 'overall risk' in this step does not take into account potential benefits of the LMO under the conditions of use[11]. Qualification of the risk estimation in determining the level of the overall risk may be expressed as, for instance, negligible, low, medium, high or indeterminate due to uncertainty or lack of knowledge, whereby it is recommended that the use of these terms has been described for instance in guidance on risk assessment published or adopted by the Party.

Points to consider:

(a) The assessments of likelihood (step 2).

(b) The evaluation of the consequences (step 3).

(c) Potential cumulative adverse effects due to the presence of multiple LMOs in the receiving environment, and synergistic/combinatorial potential adverse effects due to the presence of multiple transgenes or DNA sequences in the LMO and traits that may interact.

[11] Consideration of risks versus (environmental) benefit may be performed in the final step 5 where the acceptability of identified risks is assessed, or during decision-making.

(d) Analysis of uncertainty, conducted to characterize and address uncertainties (including variability) inherent in scientific information used in the risk assessment.

Links to BCH pages with guidance or supporting material for paragraphs of this step will be provided.

Step 5: "A recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage these risks"

Rationale: If the evaluation of the overall risk, done in the previous step, leads to the conclusion that the identified risks are not negligible, the question arises whether those risks are acceptable, and whether risk management options can be identified that have the potential to remove the identified risks or reduce its level. In the process of the formulation of risk management options, the effect of the proposed options on the identified risks should be explained. The risk assessment should then be reiterated to estimate the new levels of likelihood, consequence or risk taking into account the implementation of the risk management options.
The recommendation of acceptability of risk(s) should acknowledge the previously identified uncertainties. Some uncertainties may be addressed by monitoring (e.g. to check the validity of hypotheses in the risk assessment about the ecological effects of the LMO), requests for more information, or implementing the appropriate risk management options.

The recommendation(s) made during this step will be considered by the decision-makers in reaching their decision.

Points to consider related to the acceptability of risks:

(a) The criteria for the establishment of the acceptable/unacceptable levels of risk, or set out in the national legislation, as well as the protection goals of the Party, as defined in when setting context and scope for a risk assessment;

(b) Relevant risks posed by the use of the non-modified recipient and practices associated with its use in the potential receiving environment, providing a baseline for the comparison with the LMO.

Points to consider related to the RM strategies:

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

(d) Ability 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 hypothesis and cause/effect relationship as well as general monitoring) including plans for appropriate contingency measures to be applied in case the results from monitoring call for them;

(e) Management options in the context of the intended use (e.g. mitigating the effect of an LMO producing insecticidal proteins, by the use of refuge areas to minimize the development of resistance against these proteins).

Links to BCH pages with guidance or supporting material for paragraphs of this step will be provided.

Relevant related issues

These issues include, among others, a number of Articles of the Protocol that are relevant and related to risk assessment or the decision-making procedure, but that are not part of the risk assessment process, as well as other issues:

- **Article 14: Bilateral, regional and multilateral agreements and arrangements**
- **Article 17: Unintentional transboundary movement and emergency measures**
- **Article 22: Capacity building**
- **Article 23: Public awareness and participation**
- **Article 26: Socio-economic considerations**
- **Article 27: Liability and Redress**

Further issues that are frequently mentioned in relation to LMO risk assessment, but that are not within the scope of Annex III of the Protocol, and are therefore not dealt with in the Roadmap, are:

- **Ethical issues.**
- **Effects on human health in the context of food or feed safety, taking into account consumer practices, patterns and habits**
- **Coexistence**