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CONFERENCE OF THE PARTIES TO THE CONVENTION  
ON BIOLOGICAL DIVERSITY SERVING AS THE  
MEETING OF THE PARTIES TO THE CARTAGENA  
PROTOCOL ON BIOSAFETY

Fifth meeting

Nagoya, Japan, 11-15 October 2010

Item 13 of the provisional agenda\*

### **RISK ASSESSMENT AND RISK MANAGEMENT (ARTICLES 15 AND 16)**

*Note by the Executive Secretary*

#### **I. INTRODUCTION**

1. The Cartagena Protocol on Biosafety sets out provisions on risk assessment (Article 15 and Annex III) to identify and evaluate possible adverse effects of living modified organisms on the conservation and sustainable use of biodiversity, taking also into account risks to human health and risk management (Article 16) to enable Parties establish and maintain appropriate mechanisms, measures and strategies to regulate, manage and control risks identified in the risk assessment process according to provisions of the Protocol.

2. At its first meeting, the Conference of the Parties serving as the meeting of the Parties to the Protocol decided to consider at its fifth meeting a modality that might enable the identification of living modified organisms that are not likely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, with a view to arrive at a decision in accordance with paragraph 4 of Article 7.<sup>1</sup>

3. At their fourth meeting, in considering the need for further guidance on specific aspects of risk assessment and risk management, the Parties established an open-ended online forum on specific aspects on risk assessment through the Biosafety Clearing-House (BCH) and an Ad Hoc Technical Expert Group on Risk Assessment and Risk Management (AHTEG) with the terms of reference as annexed to the decision. In addition, the Parties to the Protocol requested the Executive Secretary to convene: (i) ad hoc discussion groups and at least one real-time online conference per region prior to each of the meetings of the AHTEG, with the view to identifying major issues related to specific aspects of risk assessment and

\* UNEP/CBD/BS/COP-MOP/5/1.

<sup>1</sup> Paragraph 7 (a) (i) of the annex to decision BS-I/12.

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risk management as referenced in the annex to the decision; and (ii) two meetings of the AHTEG prior to the fifth meeting of the Conference of the Parties serving as the meeting of the Parties to the Protocol.<sup>2</sup>

4. In their consideration of capacity-building in risk assessment, the Parties, at their fourth meeting, further requested the Executive Secretary to: (i) coordinate and facilitate, along with other relevant United Nations bodies and other international organizations, the development of training on risk assessment and risk management in relation to living modified organisms; (ii) convene prior to the fifth meeting of the Parties, regional or subregional training courses to enable countries to gain hands-on experience in preparing and evaluating reports of risk assessments in accordance to the Protocol; and (iii) convene a workshop on capacity-building and exchange of experiences on risk assessment and risk management of living modified organisms in the Pacific subregion.<sup>3</sup>

5. In addition to addressing the need for further guidance on specific aspects of risk assessment as noted in paragraph 3, and in accordance with its terms of reference as set out by the Parties, the AHTEG was also requested to consider possible modalities for cooperation in identifying living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health. To assist the AHTEG in its deliberations, the Conference of the Parties serving as the meeting of the Parties to the Protocol requested Parties and invited other Governments and relevant organizations to submit scientifically sound information available, on the identification of living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health. The Parties also requested the Executive Secretary to compile the information received and to prepare a synthesis report for consideration by the AHTEG and the Parties.<sup>4</sup>

6. Accordingly, this note is prepared by the Executive Secretary to assist the Parties to the Protocol in their consideration of the agenda item on risk assessment and risk management. Section II contains an analysis of the main outcomes of the process for the development of further guidance on specific aspects of risk assessment. Section III contains an overview of the capacity-building activities undertaken in response to the requests of the meeting of the Parties. Section IV contains an overview of the submissions and recommendations regarding collaboration in identifying living modified organisms that *may have an adverse effect* on the conservation and sustainable use of biological diversity, taking also into account risks to human health.<sup>5</sup> Section V provides some elements that may assist Parties in considering modalities for identifying living modified organisms that *are not likely to have adverse effects* on the conservation and sustainable use of biological diversity, taking also into account risks to human health.<sup>6</sup> Section VI derives some conclusions and proposes some elements of a draft decision for the consideration of the Parties.

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<sup>2</sup> Paragraphs 3, 4 and 6 of decision BS-IV/11.

<sup>3</sup> Paragraphs 12 and 13 of decision BS-IV/11.

<sup>4</sup> Paragraphs 3, 4 and 6 of decision BS-IV/11.

<sup>5</sup> As per paragraph 4 (b) (iii) of the annex to decision BS-I/12.

<sup>6</sup> As per paragraph 7 (a) (i) of the annex to decision BS-I/12.

## II. FURTHER GUIDANCE ON SPECIFIC ASPECTS OF RISK ASSESSMENT

7. To implement the various elements of decision BS-IV/11 with regard to the development of further guidance on risk assessment, the Secretariat, in consultation with the Bureau of the Conference of the Parties serving as the meeting of the Parties to the Protocol, established a continuous process comprising three types of activities: (i) ad hoc online discussion groups; (iii) regional real-time online conferences; and (iv) face-to-face meetings of the AHTEG.

8. The process was initiated with the opening of the Open-ended Online Expert Forum on Risk Assessment and Risk Management (Online Forum) through the Biosafety Clearing-House.<sup>7</sup>

9. In a notification, the Executive Secretary invited Parties, other Governments and relevant organizations to nominate experts in risk assessment to the Online Forum by using the common format for nomination of Biosafety Experts. The Secretariat reviewed the nominations for completeness in accordance with the criteria and minimum requirements for biosafety experts as set out in decision BS-IV/4.

10. A total of 229 experts were registered in the Open-ended Online Forum. Among these, 153 experts were nominated by a total of 48 Parties, 11 experts by a total of five non-Parties and 65 experts registered as observers.<sup>8</sup>

11. As part of the preparation for the work of the AHTEG, eight ad hoc online discussion groups and four regional real-time online conferences (Europe, Latin America, Africa and Asia) were held under the Online Forum between November 2008 and February 2009.<sup>9</sup>

12. Participants for the AHTEG were selected on the basis of their active participation in the events of the Online Forum, in accordance with the consolidated *modus operandi* of the Subsidiary Body on Scientific, Technical and Technological Advice (SBSTTA) of the Convention on Biological Diversity,<sup>10</sup> as requested in decision BS-IV/11 and in consultation with the Bureau of the Conference of the Parties serving as the meeting of the Parties to the Protocol. The list of participants of the AHTEG is attached hereto as annex I.

13. The first meeting of the AHTEG on Risk Assessment and Risk Management was held in Montreal from 20 to 24 April 2009. Eighteen participants from seventeen Parties, as well as eight observers from three non-Parties and five organizations attended the meeting as members of the AHTEG.

14. Between the two meetings held by the AHTEG, a number of activities took place with the view to advancing the draft of the guidance on each of the specific issues identified in the first meeting of the AHTEG and to test the Roadmap as mandated by the Parties, as follows:

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<sup>7</sup> Available at [http://bch.cbd.int/onlineconferences/forum\\_RA.shtml](http://bch.cbd.int/onlineconferences/forum_RA.shtml).

<sup>8</sup> The list of participants is available at: [http://bch.cbd.int/onlineconferences/participants\\_ra.shtml](http://bch.cbd.int/onlineconferences/participants_ra.shtml).

<sup>9</sup> The full transcripts of the discussion groups are available at: [http://bch.cbd.int/onlineconferences/archived\\_discussions\\_ra.shtml](http://bch.cbd.int/onlineconferences/archived_discussions_ra.shtml). The documents and full transcripts of the Real-time Online Conferences are available at: [http://bch.cbd.int/onlineconferences/realtime\\_ra.shtml](http://bch.cbd.int/onlineconferences/realtime_ra.shtml).

<sup>10</sup> Paragraph 18 of annex III to decision VIII/10 of the Conference of the Parties.

(a) *Under the Open-ended Online Forum:* ten ad hoc discussion groups and four regional real-time online conferences (Africa, Asia and the Pacific, WEOG and CEE, and GRULAC);<sup>11</sup> and

(b) *Under the AHTEG:* five rounds of online discussions groups, two teleconferences of the AHTEG Bureau, and face-to-face meetings of the Sub-Working Group on the Roadmap and AHTEG Bureau.<sup>12</sup>

15. The activities listed in paragraph 14 above alternated between the Open-ended Online Expert Forum and the AHTEG in order to create a feedback loop for each new draft version of the guidance documents prepared by the AHTEG sub-working groups and to enable the participation of a broad number of experts throughout the process.

16. The second meeting of the AHTEG took place from 20 to 24 April 2010 in Ljubljana, Slovenia. The meeting was attended by fourteen members of the AHTEG from Parties, as well as two members from non-Parties and four from organizations.

17. A complete list of activities carried out under the Online Forum and AHTEG is attached hereto as annex II.

**A. *Outcomes of the Open-ended Online Expert Forum on Risk Assessment and Risk Management***

18. Recommendations from the Online Forum to the AHTEG prior to its first meeting were on the following:

(a) The development of guidance on the following specific aspects of risk assessment and risk management: (i) living modified fish, trees, microorganisms and pharmaplants; (ii) living modified organisms with stacked genes or traits; (iii) specific receiving environments; and (iv) post-release monitoring and long-term effects of living modified organisms released into the environment; and

(b) An action plan for the development of guidance materials on specific prioritized aspects as well as the roadmap.

19. After the first meeting of the AHTEG, the discussions under the Open-ended Online Expert Forum assisted in advancing the draft and testing of the Roadmap, as well as in developing the guidance on specific aspects of risk assessment that were identified by the AHTEG as priorities (i.e. living modified mosquitoes, living modified crops with tolerance to abiotic stress and living modified organisms with stacked genes).

20. During several rounds of discussions, Experts of the Online Forum provided substantial input to the AHTEG on the contents of the Roadmap and specific aspects of risk assessment. In testing the Roadmap, the majority of views were positive about its usefulness and relevance, and several recommendations were made on ways to improve the user-friendliness of the Roadmap.

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<sup>11</sup> The full transcripts of the discussion groups are available at: [http://bch.cbd.int/onlineconferences/archived\\_discussions\\_ra.shtml](http://bch.cbd.int/onlineconferences/archived_discussions_ra.shtml). The documents and full transcripts of the Real-time Online Conferences are available at: [http://bch.cbd.int/onlineconferences/realtime\\_ra.shtml](http://bch.cbd.int/onlineconferences/realtime_ra.shtml).

<sup>12</sup> The meetings of the Sub-Working Group on the Roadmap and AHTEG Bureau were held in The Hague from 12 to 14 October 2009.

21. During the last round of ad hoc discussion groups, members of the Online Forum were invited to make recommendations to the meeting of the Parties for its consideration at its fifth meeting on the way forward for the risk assessment and risk management processes. Forum participants expressed views on the usefulness of the Roadmap and guidance on specific aspects of risk assessment and noted that these documents should be regularly revised and updated in order ensure its relevance and keeping in tune with new developments.

22. The participants of the Online Forum also noted the need for the development of additional guidance on other specific aspects of risk assessment. The risk assessment topics listed in information documents UNEP/CBD/BS/COP-MOP/5/INF/12 and UNEP/CBD/BS/COP-MOP/5/INF/13 were noted by the Forum as a starting point for the development of further guidance.<sup>13</sup> In addition participants also recommended that the following topics be considered: (i) establishing risk scenarios; (ii) risk management strategies, including post-release monitoring of the impacts of living modified organisms released into the environment; (iii) uncertainty and variability analysis; (iv) a “checklist” containing critical elements of the risk assessment process; and (v) how to better link the risk assessment process under the Protocol to provisions and decisions under the Convention on Biological Diversity.

23. It was further recommended during the Online Forum discussions that, in developing new guidance, consultation among Parties should be continued and that existing guidance developed by other international bodies (e.g., OECD, IPPC) should be taken into consideration.

24. With regard to a mechanism to address the development of further guidance, a large number of experts recommended an AHTEG, online discussions and information exchange through the BCH, or a combination of these. Additional examples of mechanisms to address the development of guidance included consultation among experts and a pool of resource experts to implement follow-up training once the guidance is developed.

25. The views and recommendations made under the Open-ended Online Expert Forum are synthesized and made available as information documents for consideration by the Parties (UNEP/CBD/BS/COP-MOP/5/INF/12 and 14).<sup>14</sup>

### ***B. Outcomes of the Ad Hoc Technical Expert Group on Risk Assessment and Risk Management***

26. The main outcomes of the first meeting of the AHTEG were (i) a draft of the Roadmap; (ii) identification and prioritization of three other specific issues of risk assessment (i.e. living modified mosquitoes, living modified crops with tolerance to abiotic stress and living modified organisms with stacked genes) for the development of guidance; (iii) establishment of four sub-working groups to focus on each of the issues identified; and (iv) development of an action plan made up of a summary of the terms and procedures for the development of guidance prior to the second meeting of the AHTEG.

27. During its intersessional period, in consultations with the Open-ended Online Expert Group, the AHTEG sub-working groups further developed the draft documents for guidance on the four specific issues of risk assessment and tested the draft Roadmap for Risk Assessment of Living Modified Organisms.

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<sup>13</sup> Available at <http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018>.

<sup>14</sup> Information documents UNEP/CBD/BS/COP-MOP/5/INF/12 and UNEP/CBD/BS/COP-MOP/5/INF/14 are available at <http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018>.

28. At its second meeting, the main outcomes of the AHTEG were:

(a) Finalization of the document entitled “Guidance on Risk Assessment of Living Modified Organisms” and divided into two sections entitled “Part I: Roadmap for Risk Assessment of Living Modified Organisms” and “Part II: Specific Types of Living Modified Organisms and Traits” (i.e. living modified crops with tolerance to abiotic stress, living modified mosquitoes and living modified organisms with stacked genes or traits). This document is attached hereto as annex III and will also be made available through the BCH;<sup>15</sup>

(b) Recommendations to the Secretariat on how to integrate and update the guidance document produced by the AHTEG and tools for retrieval of background materials available in the Biosafety Information Resources Centre of the BCH; and

(c) An assessment of the action plan established at its first meeting.

29. The AHTEG also made recommendations to the Parties at their fifth meeting for further development of guidance on additional topics of risk assessment, particularly on those specific issues of risk assessment that were identified and prioritized during the Open-ended Online Forum and first meeting of the AHTEG.

30. The report of the first meeting and final report of the AHTEG are available as information documents for consideration by the Parties.<sup>16</sup>

31. The full set of recommendations from the AHTEG to the fifth meeting of the Parties is attached hereto as annex IV.

### III. CAPACITY-BUILDING IN RISK ASSESSMENT

32. In response to the request by the Parties on capacity-building in risk assessment, the Secretariat coordinated a multi-stakeholder process for the development of training in collaboration with United Nations organizations (Aarhus Convention of the United Nations Economic Commission for Europe, International Plant Protection Convention of the Food and Agriculture Organization of the United (FAO) and the United Nations Environment Programme (UNEP)), other international organizations (Global Industry Coalition and Third World Network) and the academic sector (University of Canterbury and University of Minnesota).

33. The development of training was undertaken in a step-wise manner. The Secretariat first prepared an outline of the training and invited collaborators to provide input and comments. Thereafter, on the basis of the various feedbacks, the Secretariat prepared a draft training manual and invited the collaborators for peer-review. The draft manual was then revised by the Secretariat on the basis of the feedback and comments provided during the peer-review process.

34. While using the provisions of the Cartagena Protocol on Biosafety, particularly its Annex III, as a basis for drafting and reviewing the emerging training manual, the Secretariat also attempted to incorporate experience and current practice from number of national regulatory frameworks and international organizations in a comprehensive manner.

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<sup>15</sup> Available at [http://bch.cbd.int/onlineconferences/forum\\_RA.shtml](http://bch.cbd.int/onlineconferences/forum_RA.shtml).

<sup>16</sup> Information documents UNEP/CBD/BS/COP-MOP/5/INF/13 and UNEP/CBD/BS/COP-MOP/5/INF/15 are available at <http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018>.

35. The outcome of this process is a draft training manual entitled “Risk Assessment of Living Modified Organisms”, which comprises four modules: (i) Overview of Biosafety and the Cartagena Protocol on Biosafety; (ii) Preparatory Work – Understanding the Context in which a Risk Assessment is Carried Out; (iii) Conducting the Risk Assessment; and (iv) Preparing a Risk Assessment Report.

36. The training manual is available as an information document and through the BCH for consideration by the Parties.<sup>17</sup>

37. To further address the request of the Parties to convene capacity-building activities with the view to enabling countries to exchange experience and gain hands-on knowledge in preparing and evaluating risk assessment reports in accordance with the Protocol, the training manual described above was used during the following activities:

(a) The Pacific subregional workshop on capacity-building and exchange of experiences on risk assessment in Nadi, Fiji, from 4 to 7 July 2010; and

(b) The Asian subregional training course on risk assessment of living modified organisms in Siam Reap, Cambodia, from 12 to 16 July 2010.

38. Twelve participants from six Parties to the Protocol (Fiji, Kiribati, Niue, Samoa, Solomon Islands and Tonga), two non-Party countries (Cook Islands and Vanuatu) and one organization (University of Canterbury, New Zealand) attended the Pacific subregional workshop. Twenty-three participants from fifteen Parties to the Protocol (Bhutan, Cambodia, India, Indonesia, Islamic Republic of Iran, Lao People’s Democratic Republic, Malaysia, Mongolia, Myanmar, Pakistan, Syrian Arab Republic, Thailand, Turkmenistan, Viet Nam and Yemen), a non-governmental organization (Third World Network) and the United Nations Environmental Programme attended the training course for Asia. One resource person from the Netherlands also took part in the Asian training course.

39. Participants were invited to answer a questionnaire to evaluate the Pacific workshop and the Asian training course. Results of the questionnaire indicated a general agreement that these activities (i) provided hands-on training in preparing and evaluating risk assessment reports in accordance to the articles and Annex III of the Protocol; (ii) helped develop skills on how to use and interpret existing information, as well as identifying and addressing information gaps; and (iii) helped to understand how to establish baseline information relevant for the risk assessment.

40. Results of the questionnaire also indicated that the majority of participants agreed that the training manual prepared by the Secretariat in collaboration with other United Nations bodies and relevant organizations (i) is a useful tool for training on risk assessment; (ii) is easy to understand in a stepwise manner; (iii) comprises an adequate overview of the risk assessment process, and (iv) is useful for a wide range of users.

41. In providing further feedback, participants considered the training manual a very good teaching tool that provides a well-structured and comprehensive introduction to the risk assessment process and is useful to Parties as well as to other countries and relevant organizations. With the view to improving its usefulness, participants noted that the training manual should:

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<sup>17</sup> The training manual is available as information document UNEP/CBD/BS/COP-MOP/5/INF/22 at <http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018> and through the Biosafety Clearing-House at [http://bch.cbd.int/protocol/cpb\\_art15/training](http://bch.cbd.int/protocol/cpb_art15/training).

(a) Be further improved by, *inter alia*, adding a glossary of terms, list of acronyms, flowcharts, diagrams, examples of other non-crop living modified organisms, etc;

(b) Integrate elements from the “Guidance on Risk Assessment of Living Modified Organisms” developed by the AHTEG, namely from the Roadmap (e.g. flowchart) and from the guidance on the specific types of living modified organisms and traits (i.e. risk assessment of living modified mosquitoes, living modified organisms with stacked genes or traits and living modified crops with tolerance to abiotic stress); and

(c) Be presented through a more user-friendly learning tool (e.g. as an interactive software); and

(d) Be published in all United Nations languages.

42. The participants to the Pacific workshop and Asian training course agreed that the following elements/activities could be considered by the Parties at their fifth meeting:

*Capacity-building on risk assessment:*

(a) Further training courses on risk assessment at the national level or for smaller geographical areas (e.g. around 5-7 countries) where the receiving environment is similar to allow the participation of a core team of country experts per country;

(b) Follow-up advance training in risk assessment focusing, for example, on different types of intended uses (i.e. introduction into the environment and living modified organisms for direct use as food, feed, or for processing) and different types of living modified organisms;

(c) Dedicated training courses on: (i) preparing risk assessment reports and recommendations; (ii) extracting relevant data from notifications; (iii) assessing the quality of data submitted the application; and (iv) establishing detailed baseline information;

(d) Training of trainers who can further carry out capacity-building at national level;

*Guidance on risk assessment:*

(e) Publication and distribution of the AHTEG “Guidance on Risk Assessment of Living Modified Organisms”, including an online version on the Biosafety Clearing-House, in all United Nations languages;

(f) Development of further guidance on risk assessment as recommended by the AHTEG;

*General capacity-building on biosafety:*

(g) Further regional training on the identification of living modified organisms; and

(h) Training of decision-makers on the interpretation of recommendations of the risk assessment and on the implementation of risk management strategies.

43. The reports of these capacity-building activities are available as information documents for consideration by the Parties (UNEP/CBD/BS/COP-MOP/5/INF/16 and 17).<sup>18</sup>

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<sup>18</sup> Information documents UNEP/CBD/BS/COP-MOP/5/INF/16 and UNEP/CBD/BS/COP-MOP/5/INF/17 are available at <http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018> .



**IV. COLLABORATION IN IDENTIFYING LIVING MODIFIED ORGANISMS OR SPECIFIC TRAITS *THAT MAY HAVE ADVERSE EFFECTS ON THE CONSERVATION AND SUSTAINABLE USE OF BIOLOGICAL DIVERSITY, TAKING ALSO INTO ACCOUNT RISKS TO HUMAN HEALTH***

44. In a notification, the Executive Secretary invited Parties, other Governments and relevant organizations to submit scientifically sound information on the identification of living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health.<sup>19</sup>

45. In some submissions received by the Secretariat, references were made to living modified organisms or specific traits that may have adverse effects such as living modified cotton, fish, maize, trees, viruses, as well as living modified organisms for production of pharmaceutical compounds, with stacked genes or traits, insect resistance, tolerance to abiotic stress and pesticides, modified nutrient uptake or harboring antibiotic resistance marker genes. Some submissions, on the other hand, noted that there is no science-based evidence pointing at potential adverse effects of living modified organisms commercialized to date.

46. On the basis of the submissions above, the Secretariat prepared a “Compilation of submissions on the identification of living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health” for consideration by the AHTEG and the Parties.<sup>20</sup>

47. After deliberations on this issue, the AHTEG identified the following modalities for cooperation: (i) exchange of information via the Biosafety Clearing-House; (ii) workshops; (iii) an ad hoc technical expert group; and (iv) cooperation in the testing of living modified organisms.

48. A number of members of the AHTEG also agreed that a step-wise process could be established for this purpose, in which an initial phase of information gathering would be followed by a second phase for the analysis of the information.

49. The AHTEG made further specific recommendations regarding this issue as shown in paragraphs (f) and (g) (iv) of annex IV below.

**V. IDENTIFICATION OF LIVING MODIFIED ORGANISMS *THAT ARE NOT LIKELY TO HAVE ADVERSE EFFECTS ON THE CONSERVATION AND SUSTAINABLE USE OF BIOLOGICAL DIVERSITY, TAKING ALSO INTO ACCOUNT RISKS TO HUMAN HEALTH***

50. Paragraph 4 of Article 7 to the Protocol states that “the advance informed agreement procedure shall not apply to the intentional transboundary movement of living modified organisms identified in a decision of the Conference of the Parties serving as the meeting of the Parties to this Protocol as being not likely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health”.

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<sup>19</sup> Notification SCBD/BS/MPDM/jh/67587 (2009-056) available at <http://bch.cbd.int/protocol/notifications/>.

<sup>20</sup> Available as information document UNEP/CBD/BS/COP-MOP/5/INF/11 at: <http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018>.

51. In its deliberations on modalities that might enable the identification of living modified organisms that are not likely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, the Parties at their fifth meeting may take into consideration, *inter alia*, the following submissions made by Parties through the BCH under the simplified procedure (Article 13) in which the imports of living modified organisms were exempted from the advanced informed agreement procedure.<sup>21</sup>

52. As of 10 June 2010, the following living modified organisms were submitted to the BCH under the simplified procedure:

<b>LMO for which the simplified procedure was applied</b>	<b>Country</b>	<b>BCH Record</b>
Bollgard™ Cotton	Colombia	8151
Roundup Ready™ Cotton	Colombia	8155
Bollgard II™ Cotton (MON-15985-7)	South Africa	5666
Bollgard™ cotton (MON-00531-6)	South Africa	5679
YieldGard™ Maize (MON-00810-6)	South Africa	5712
YieldGard™ Maize (SYN-BT011-1)	South Africa	5715
Roundup Ready™ Maize (MON-00603-6)	South Africa	8164
Roundup Ready™ Soybean (MON-04032-6)	South Africa	8167
Roundup Ready™ Cotton (MON-01445-2)	South Africa	8170
Roundup Ready™ YieldGard™ Maize (MON-00603-6 x MON-00810-6)	South Africa	40513
Roundup Ready™ Flex™ Cotton (MON-88913-8)	South Africa	40514
Roundup Ready™ Bollgard™ Cotton (MON-00531-6 x MON-01445-2)	South Africa	40516

## **VI. CONCLUSIONS AND ELEMENTS OF A DRAFT DECISION**

### **A. Further guidance on specific aspects of risk assessment**

53. The tasks mandated by the Parties in the terms of reference for the Online Forum and AHTEG for the development of further guidance on risk assessment were successfully carried out through a process that included both online and face-to-face deliberations.

54. A large group of experts deliberated online through ad hoc discussion groups and real-time conferences and made recommendations to a smaller group, the AHTEG, that met face-to-face. This process enabled a large number of experts in various scientific and technical fields relevant to risk assessment to provide input into the development of the guidance material in a cost effective manner under the limited financial resources available.

<sup>21</sup> Article 13, paragraph 1 (b).

55. An outcome of this process is a document entitled “Guidance on Risk Assessment of Living Modified Organisms”. The AHTEG and Online Forum recommended that this guidance document should be (i) published and distributed, including an online version under the BCH, in all United Nations languages; (ii) further tested for example during regional workshops including cooperation with existing initiatives for capacity-building and training, as appropriate; and (iii) revisited within two years and the need for an update of the list of background materials should be assessed within a year.

56. While significant progress towards addressing the need for guidance on risk assessment was made with the development of the document above, many members of the AHTEG and Online Forum were of the view that further development of guidance is still needed and therefore recommended that the process of combining an Online Forum and an AHTEG should be continued.

57. Based on the above information and taking into account, *inter alia*, the recommendations of the Online Forum and AHTEG, the Conference of the Parties serving as the meeting of the Parties to the Protocol may wish to:

(a) Support and endorse the continuation of the work of both the Open-ended Online Expert Forum and the AHTEG on Risk Assessment and Risk Management, to (i) develop additional guidance on specific types of living modified organisms and traits, taking into account, *inter alia*, the topics listed in annex V below; and (ii) revise the text of the “Guidance on Risk Assessment of Living Modified Organisms”, for instance, on the basis of the testing of the guidance during capacity-building activities, and update its lists of background materials;

(b) Request the Executive Secretary to: (i) publish and distribute it in all United Nations languages the document “Guidance on Risk Assessment of Living Modified Organisms”, including an online version on the Biosafety Clearing-House (BCH); (ii) test the guidance document during regional workshops including cooperation with existing initiatives for capacity-building and training, as appropriate; (iii) revise the common format for submission of records to the Biosafety Information Resources Centre (BIRC) of the BCH in order to link BIRC records on risk assessment to specific sections of the guidance document;

(c) Continue the discussions under the Open-ended Online Expert Forum on Risk Assessment and Risk Management and request the Executive Secretary to extend the invitation for additional experts;

(d) Establish an Ad Hoc Technical and Expert Group on Risk Assessment and Risk Management and request the Executive Secretary to apply the same *modus operandi* in the selection of experts as in the previous process.

### ***B. Capacity-building in risk assessment***

58. With regard to capacity-building, a training manual was developed in collaboration with some relevant UN organizations and international organizations. The manual was used as a basis for capacity-building activities that took place for the Pacific and Asia subregions. The participants of the workshop and training course made several recommendations with regards to improving the training manual for its usefulness and user friendliness. Furthermore, the participants recommended that the manual be developed as an interactive training material (e.g. CD-ROM), translated and distributed in all UN languages.

59. Based on the above information and taking into account, *inter alia*, the recommendations of the participants of the capacity-building activities, the Conference of the Parties serving as the meeting of the Parties to the Protocol may wish to:

(a) Request the Executive Secretary to convene, at the earliest convenient date and subject to the availability of funds, further regional or sub-regional training courses to enable countries to gain hands-on experience in the preparation and evaluation of risk assessment reports in accordance to the articles and Annex III of the Protocol;

(b) Further request the Executive Secretary, in cooperation with relevant United Nations and other organizations, to improve the usefulness of the training manual "Risk Assessment of Living Modified Organisms" by: (i) regularly revising it on the basis of the recommendations provided during the regional and sub-regional capacity-building activities; (ii) developing it into an interactive learning tool, such as a CD-ROM and make them available through the BCH; and (iii) publishing and distributing the manual to Parties, other Governments and relevant organizations.

**C. *Identifying living modified organisms or specific traits that (i) may have or (ii) are not likely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health***

60. Divergent views were expressed by Parties, other Governments and relevant organizations with regards to the identification of living modified organisms or specific traits that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health. The AHTEG identified the following modalities for addressing the issue: (i) exchange of further information through the Biosafety Clearing-House; (ii) workshops; (iii) an ad hoc technical expert group; and (iv) cooperation in assessing potential adverse effects of living modified organisms. This process could be initiated in a stepwise manner by first phase of gathering information then followed by the analysis of the information.

61. With regard to the identification of living modified organisms that are not likely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, the Parties may take note, *inter alia*, of the decisions taken under the Simplified Procedure on imports of living modified organisms exempted from the advanced informed agreement procedure and submitted to the BCH.

62. Based on the above information and taking into account, *inter alia*, the views expressed by Parties, other Governments and relevant organizations and recommendations of the Open-ended Online Forum and AHTEG, the Conference of the Parties serving as the meeting of the Parties to the Protocol may wish to establish one or more mechanisms including, for instance, exchange of information, workshops and/or an expert group with the view to enabling Parties to take decisions on identifying living modified organisms or specific traits that (i) *may have* or (ii) *are not likely to have* adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health.

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*Annex II*

**ACTIVITIES CARRIED OUT UNDER THE OPEN-ENDED ONLINE EXPERT GROUP ON RISK ASSESSMENT AND RISK MANAGEMENT AND BY THE AD HOC TECHNICAL EXPERT GROUP ON RISK ASSESSMENT AND RISK MANAGEMENT**

Activity	Date / Location
Opening of the Online Forum and announcement of the topics and calendar of the discussion groups	6 November 2008, online
Ad hoc discussion groups under the Open-ended Online Forum on risk assessment and risk management of: (i) living modified (LM) fish; (ii) LM trees; (iii) LM microorganisms and viruses; (iv) LM pharmaplants; (v) living modified organisms (LMOs) with stacked genes or traits; (vi) post-release monitoring and long-term effects of LMOs released into the environment; and (vi) specific receiving environments; as well as on a Flowchart ("Roadmap") for risk assessment: the necessary steps to conduct risk assessment according to Annex III of the Protocol	10 November – 19 December 2008, online
First Series of Regional Real-time Online Conferences (for Europe, Latin America, Africa and Asia)	28 January – 17 February 2009, online
First Meeting of the Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management	20 – 24 April 2009, Montreal, Canada
Meeting of the AHTEG Bureau.	24 April 2009, Montreal, Canada
Ad hoc discussion groups within the AHTEG sub-working groups for further drafting of the guidance documents	May – June 2009, online
Ad hoc discussion groups under the Open-ended Online Forum for input to the work of the AHTEG Sub-working Groups	22 June – 12 July 2009, online
Teleconference of the AHTEG Bureau	24 July 2009
Ad hoc discussion groups within the AHTEG sub-working groups for further drafting of the guidance documents and testing of the Roadmap	August – October 2009, online
Progress reports on the work of the AHTEG sub-working groups	October 2009
Meetings of the AHTEG Sub-Working Group on the Roadmap and AHTEG Bureau	12 – 14 October 2009, The Hague, Netherlands
Ad hoc discussion groups within the AHTEG sub-working groups for further drafting of the guidance documents and testing of the Roadmap	November 2009, online
Ad hoc discussion groups under the Open-ended Online Forum for further input to the work of the AHTEG sub-working groups	23 November – 14 December 2009, online

Activity	Date / Location
Ad hoc discussion group under the Open-ended Online Forum on “The way forward for the development of further guidance on risk assessment and risk management of LMOs”	7 – 14 December 2009
Ad hoc discussion groups within the AHTEG sub-working groups for further drafting of the guidance documents	January 2010, online
Second series of Regional Real-time Online Conferences (for Africa, Asia and the Pacific, WEOG and CEE, and Latin America and the Caribbean)	2-11 February 2010, online
Ad hoc discussion group under the AHTEG for final drafting of the guidance documents in preparation for the second AHTEG meeting	March 2010, online
Teleconference of the AHTEG Bureau	7 April 2010
Preparatory meetings of the AHTEG sub-working groups	19 April 2010, Ljubljana
Second meeting of the Ad Hoc Technical Expert Group	20-23 April 2010, Ljubljana

*Annex III*

**GUIDANCE ON RISK ASSESSMENT OF LIVING MODIFIED ORGANISMS**

1 This document was developed by the Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment  
2 and Risk Management under the Cartagena Protocol on Biosafety.<sup>22</sup>

3 This is intended to be a “living document” that will be improved with time as new experience becomes  
4 available and new developments in the field of applications of living modified organisms (LMOs) occur,  
5 as and when mandated by the Parties to the Cartagena Protocol on Biosafety.

6 **PART I:**

7 **ROADMAP FOR RISK ASSESSMENT OF LIVING MODIFIED ORGANISMS**

8 This “Roadmap” provides an overview of the process of environmental risk assessment for a living  
9 modified organism (LMO) in accordance with Annex III<sup>23</sup> to the Cartagena Protocol on Biosafety  
10 (hereinafter “the Protocol”) and all other articles related to risk assessment. This Roadmap was  
11 developed in response to decision BS-IV/11<sup>24</sup> of the Conference of the Parties serving as the meeting of  
12 the Parties to the Protocol (COP-MOP). Annex III is the basis of the Roadmap. Accordingly, this  
13 Roadmap is a guidance document and does not replace Annex III. The overall aim of the Roadmap is  
14 facilitating and enhancing the effective use of Annex III by elaborating the technical and scientific  
15 process of how to apply the steps and points to consider in the process of risk assessment.

16 The purpose of this Roadmap is to provide further guidance on using Annex III with additional  
17 background material and links to useful references relevant to risk assessment. The Roadmap may be  
18 useful as a reference for risk assessors when conducting or reviewing risk assessments and in  
19 capacity-building activities.

20 The Roadmap applies to all types of LMOs<sup>25</sup> and their intended uses within the scope and objective of  
21 the Protocol, and in accordance with Annex III. However, it has been developed based largely on living  
22 modified crop plants because of the extensive experience to date with environmental risk assessments for  
23 these organisms. It is intended to be a “living document” that will be modified and improved on over  
24 time as and when mandated by COP-MOP, and in the light of new experience, information and  
25 developments in the field of applications of LMOs, e.g. when other types of LMOs have been evaluated  
26 more extensively in environmental risk assessments.

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<sup>22</sup> The AHTEG on Risk Assessment and Risk Management was established by the Conference of the Parties serving as the meeting of the Parties to the Cartagena Protocol on Biosafety (COP-MOP) in its decision BS-IV/11. The terms of reference for the AHTEG as set out by the Parties may be found in the annex to decision BS-IV/11 (<http://bch.cbd.int/protocol/decisions/decision.shtml?decisionID=11690>).

<sup>23</sup> <http://www.cbd.int/biosafety/articles.shtml?a=cpb-43> .

<sup>24</sup> <http://www.cbd.int/biosafety/cop-mop/results/?id=11690> .

<sup>25</sup> Including products thereof, as described in paragraph 5 of Annex III to the Protocol.

27 **INTRODUCTION**

28 **General introduction**

29 *Background*

30 In accordance with the precautionary approach<sup>26</sup> the objective of the Protocol is “to contribute to  
31 ensuring an adequate level of protection in the field of the safe transfer, handling and use of LMOs  
32 resulting from modern biotechnology that may have adverse effects on the conservation and sustainable  
33 use of biological diversity, taking also into account risks to human health, specifically focusing on  
34 transboundary movements”.<sup>27</sup>

35 For this purpose, Parties shall ensure that risk assessments are carried out when making informed  
36 decisions regarding LMOs.

37 An LMO and its use may have several effects, which may be intended or unintended, taking into account  
38 that some unintended effects may be predictable. The objective of risk assessment is to *identify* and  
39 *evaluate* the potential adverse effects of LMOs on the conservation and sustainable use of biological  
40 diversity in the likely potential receiving environment, taking also into account risks to human health.<sup>28</sup>  
41 The risk assessment is performed on a case-by-case basis. What is considered an adverse effect depends  
42 on protection goals and assessment end-points taken into consideration when scoping the risk assessment.  
43 The choice of protection goals by the Party could be informed by Articles 7(a), 7(b) and 8(g) and  
44 Annex 1 of the Convention on Biological Diversity.

45 According to the general principles of Annex III of the Protocol, risk assessments shall be based, at a  
46 minimum, on information provided in accordance with Article 8 and other available scientific evidence  
47 in order to identify and evaluate the possible adverse effects of LMOs on the conservation and  
48 sustainable use of biological diversity, taking also into account risks to human health.<sup>29</sup>

49 Annex III states that “risk assessment should be carried out in a scientifically sound and transparent  
50 manner, and can take into account expert advice of, and guidelines developed by, relevant international  
51 organizations. Lack of scientific knowledge or scientific consensus should not necessarily be interpreted  
52 as indicating a particular level of risk, an absence of risk, or an acceptable risk. (...) Risk assessment  
53 should be carried out on a case-by-case basis. The required information may vary in nature and level of  
54 detail from case to case, depending on the LMO concerned, its intended use and the likely potential  
55 receiving environment”.<sup>30</sup>

56 *The risk assessment process*

57 Risk assessment is a structured process. Paragraph 8 of Annex III provides a description of the key steps  
58 of the risk assessment process to identify and evaluate the potential adverse effects and manage risks.

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<sup>26</sup> “In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation” (Principle 15 of the Rio Declaration on Environment and Development) at: <http://www.unep.org/Documents/Multilingual/Default.asp?DocumentID=78&ArticleID=1163>), and in line with Articles 10.6 and 11.8 of the Protocol.

<sup>27</sup> <http://www.cbd.int/biosafety/articles.shtml?a=cpb-01> .

<sup>28</sup> Annex III, paragraph 1.

<sup>29</sup> Article 15, paragraph 1.

<sup>30</sup> Annex III, paragraphs 3, 4 and 6.

59 Paragraph 9 describes, depending on the case, points to consider in this process. The steps describe an  
60 integrated process whereby the results of one step may be relevant to other steps. Also, risk assessment  
61 may need to be conducted in an iterative manner, where certain steps may be repeated or re-examined to  
62 increase or re-evaluate the confidence in the conclusions of the risk assessment. When new information  
63 arises that could change its conclusions, the risk assessment may need to be re-examined accordingly.  
64 Similarly, the issues mentioned in the ‘overarching issues’ section below can be taken into consideration  
65 again at the end of the risk assessment process to determine whether the objectives and criteria that were  
66 set out at the beginning of the risk assessment have been met.

67 Risk assessment is done in a comparative manner, meaning that risks associated with living modified  
68 organisms should be considered in the context of the risks posed by the non-modified recipient organism  
69 in the likely potential receiving environment.<sup>31</sup> Additionally, experience with the same, or, as  
70 appropriate, similar, genotypic or phenotypic characteristics may be taken into consideration along with  
71 the non-modified recipient organism in the risk assessment of an LMO. For instance, the comparison  
72 with the (near-)isogenic or closely related non-modified recipient is used in step 1 of the risk assessment  
73 (see below) where the novel genotypic or phenotypic characteristics associated with the LMO are  
74 identified. But when the potential consequences of adverse effects are evaluated, broader experience,  
75 such as mentioned in step 3 (a), may be taken into account, when establishing a baseline. Results from  
76 experimental field trials or other environmental information and experience with the same LMO may be  
77 taken into account as information elements in a new risk assessment for that LMO. In all cases where  
78 information, including baseline data, is derived from other sources, it is important to establish the validity  
79 and relevance of the information for the risk assessment. For instance, it should be taken into account  
80 that the behavior of a transgene,<sup>32</sup> as that of any other gene, may vary because it depends on the genetic  
81 and physiological background of the recipient as well as on the ecological characteristics of the  
82 environment that the LMO is introduced into.

83 The concluding recommendations derived from the risk assessment in step 5 are required to be taken into  
84 account in the decision-making process on an LMO. In the decision-making process, other Articles of the  
85 Protocol or other relevant issues may also be taken into account and are addressed in the last paragraph  
86 of this Roadmap: ‘Related Issues’.

87 A flowchart illustrating the risk assessment process according to this Roadmap is annexed hereto.

88 (*See references relevant to “[General Introduction](#)”*).

### 89 **Overarching issues in the risk assessment process**

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

- 92 • Setting criteria for relevancy in the context of a risk assessment – e.g. data may be considered  
93 relevant if they can affect the outcome of the risk assessment.
- 94 • Establishment of scientifically robust criteria for the inclusion of scientific information.
  - 95 ○ Data should be of an acceptable scientific quality. Data quality should be consistent with  
96 the accepted practices of scientific evidence-gathering and reporting and may include

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<sup>31</sup> Annex III, paragraph 5.

<sup>32</sup> For the purpose of this document, a transgene is a nucleic acid sequence in an LMO that results from the application of modern biotechnology as described in Article 3 (i) (a) of the Protocol.

97 independent review of the methods and designs of studies. Data may be derived from a  
98 variety of sources, e.g. new experimental data as well as data from relevant peer  
99 reviewed scientific literature.

100 ○ Sound science is based on transparency, verifiability, and reproducibility (e.g. reporting  
101 of methods and data in sufficient detail, so that the resulting data and information could  
102 be confirmed independently), and on the accessibility of data (e.g. the availability of  
103 relevant, required data or information or, if requested and as appropriate, of sample  
104 material), taking into account the provisions of Article 21 of the Protocol on the  
105 confidentiality of information. The provisions of sound science serve to ensure and  
106 verify that the risk assessment is carried out in a scientifically sound and transparent  
107 manner.

108 ● Identification and consideration of uncertainty.

109 According to the Protocol, “where there is uncertainty regarding the level of risk, it may be  
110 addressed by requesting further information on the specific issues of concern or by implementing  
111 appropriate risk management strategies and/or monitoring the living modified organism in the  
112 receiving environment”.<sup>33</sup>

113 Uncertainty is inherent in the concept of risk. To date, “there is no internationally agreed  
114 definition of ‘scientific uncertainty’, nor are there internationally agreed general rules or  
115 guidelines to determine its occurrence. Those matters are thus dealt with – sometimes differently  
116 – in each international instrument incorporating precautionary measures”.<sup>34, 35</sup>

117 It should be kept in mind that uncertainty cannot always be reduced by providing additional  
118 information. For example, new uncertainties may arise as a result of the provision of additional  
119 information.

120 Considerations of uncertainty strengthen the confidence and scientific soundness of a risk  
121 assessment. In communicating the results of a risk assessment, it is important to consider and  
122 analyze in a systematic way the various forms of uncertainty that can arise at each step and in  
123 combination at step 4 of the Roadmap. An analysis of uncertainty includes considerations of its  
124 source and nature.

125 The *source(s)* of uncertainty may stem from the data/information itself and/or the choice of study  
126 design including the methods used, and the analysis of the information.

127 The *nature* of uncertainty may be described for each identified source of uncertainty arising  
128 from: (i) imperfect knowledge or lack of available information, which may be reduced with more  
129 research/information, and (ii) inherent variability.

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<sup>33</sup> Annex III, paragraph 8 (f).

<sup>34</sup> *An Explanatory Guide to the Cartagena Protocol on Biosafety*, paragraph 57 (<http://data.iucn.org/dbtw-wpd/edocs/EPLP-046.pdf>).

<sup>35</sup> Article 10, paragraph 6, of the Protocol: “Lack of scientific certainty due to insufficient relevant scientific information and knowledge regarding the extent of the potential adverse effects of a living modified organism on the conservation and sustainable use of biological diversity in the Party of import, taking also into account risks to human health, shall not prevent that Party from taking a decision, as appropriate, with regard to the import of that living modified organism intended for direct use as food or feed, or for processing, in order to avoid or minimize such potential adverse effects.”

130 (See references relevant to "[Identification and consideration of uncertainty](#)").

### 131 **Context and scoping of the risk assessment**

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

- 135 • Existing policies and strategies based on, for instance, regulations and the international  
136 obligations of the Party involved; (ii) Guidelines or regulatory frameworks that the Party has  
137 adopted; and (iii) Protection goals, assessment end-points, risk thresholds and management  
138 strategies. Setting the context and scope for a risk assessment that are consistent with these  
139 policies, strategies and protection goals may involve a process that includes risk assessors,  
140 decision-makers and various stakeholders prior to conducting the actual risk assessment;
- 141 • (i) Framing the risk assessment process; (ii) Taking into account the expected (potential)  
142 conditions of handling and use of the LMO; (iii) Taking into account customary practices and  
143 habits that could affect the protection goals or end-points; identification of relevant questions to  
144 be asked for that purpose;
- 145 • Identification of methodological and analytical requirements, including any reviewing  
146 mechanisms, that is required to achieve the objective of the risk assessment as laid down, for  
147 instance, in guidelines published or adopted by the Party that is responsible for conducting the  
148 risk assessment (i.e. typically the Party of import according to the Protocol);
- 149 • The nature and level of detail of the information required may depend on the intended use of the  
150 LMO and the likely potential receiving environment. For small scale field releases, especially at  
151 early experimental stages, less information may be available compared to the information  
152 available for large scale environmental release, and for commercial scale planting;
- 153 • Experience and history of use of the non-modified recipient, taking into account its ecological  
154 function;<sup>36</sup> and
- 155 • Establishing criteria for describing the level of the (potential) environmental adverse effects of  
156 LMOs, as well as criteria for the terms that are used to describe the levels of likelihood (step 2),  
157 the magnitude of consequences (step 3) and risks (step 4) and the manageability of risks (step 5;  
158 see risk assessment steps below).

159 (See references relevant to "[Context and scoping of the risk assessment](#)").

## 160 **THE RISK ASSESSMENT**

161 To fulfill its objective under Annex III, as well as other relevant Articles of the Protocol, risk assessment  
162 is performed in five steps, as appropriate. These five steps are indicated in Paragraph 8 (a)-(e) of  
163 Annex III and also detailed below. Their titles have been taken directly from the paragraphs 8 (a)-(e) of  
164 Annex III.

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<sup>36</sup> 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 a pollen source for pollinators and pollen feeders.

165 For each step a rationale and points to consider are provided. Some points to consider are taken from  
 166 paragraph 9 of Annex III, whereas others have been added based on generally accepted methodology of  
 167 LMO risk assessment and risk management. The relevance of each point to consider will depend on the  
 168 case being analyzed.

169 (*See references relevant to “[Risk Assessment in general](#)”*).

170 **Step 1: “An identification of any novel genotypic and phenotypic characteristics associated with**  
 171 **the living modified organism that may have adverse effects on biological diversity in the likely**  
 172 **potential receiving environment, taking also into account risks to human health.”<sup>37</sup>**

173 *Rationale:*

174 The purpose of this step is to identify biological changes resulting from the genetic modification(s),  
 175 including any deletions, compared to the non-modified organism, and identify what, if any, changes  
 176 could cause adverse effects on the conservation and sustainable use of biological diversity, taking also  
 177 into account risks to human health. This step is similar to the ‘hazard identification step’ in other risk  
 178 assessment guidance. The comparison of the LMO is performed with the non-modified recipient, or a  
 179 (near-)isogenic line or, as appropriate, with a non-modified organism of the same species, taking into  
 180 consideration the new trait(s) of the LMO.

181 In this step, scientifically plausible scenarios are identified in which novel characteristics of the LMO  
 182 could give rise to adverse effects in an interaction with the likely potential receiving environment. The  
 183 novel characteristics of the LMO to be considered can be genotypic or phenotypic, biological. They may  
 184 be intended or unintended, predicted or unpredicted. The points to consider below provide information  
 185 elements on which hazard identification can be built.

186 The type and level of detail of the information required in this step may vary from case to case depending  
 187 on the nature of the modification of the LMO and on the scale of the intended use of the LMO. For small  
 188 scale field releases, especially at early experimental stages, less information may be available and some  
 189 of the resulting uncertainty may typically be addressed by risk management measures (see step 5).

190 *Points to consider regarding the characterization of the LMO:*

191 (a) Relevant characteristics of the non-modified recipient (e.g. (i) its biological characteristics, in  
 192 particular those that, if changed, or interacting with the new gene products or traits of the LMO,  
 193 could cause changes in the behavior of the non-modified recipient in the environment in a way  
 194 that may cause adverse effects; (ii) its taxonomic relationships, (iii) its origin, centers of origin  
 195 and centers of genetic diversity); (iv) ecological function, and (v) as a component of biological  
 196 diversity that is important for the conservation and sustainable use of the biological diversity in  
 197 the context of Article 7(a) and Annex I of the Convention;

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

202 (c) Molecular characteristics of the LMO related to the modification (e.g. (a) characteristics of the  
 203 insert(s) which may include (i) gene products (intended and unintended), (ii) levels of  
 204 expression, (iii) functions, (iv) insertion site in the genome of the recipient and any effects of

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<sup>37</sup> The bold printed headings of each step are direct quotes from Annex III of the Protocol.



205 insertion, (v) stability or integrity within the genome of the recipient; (b) (i) the transformation  
206 method, (ii) the characteristics of the vector if and, as far as it is present in the LMO, including  
207 its identity, source or origin and host range) with particular attention paid to any characteristics  
208 that are related to potential adverse effects. The availability and relevance of this information  
209 may vary according to the type of application. Characteristics related to adverse effects may  
210 also result from changed expression levels of endogenous genes due to effects of a transgene or  
211 from combinatorial effects;<sup>38</sup>

212 (d) Consideration of genotypic (see point to consider (c) above) and phenotypic, biological changes  
213 in the LMO, either intended or unintended, in comparison with the non-modified recipient,  
214 considering those changes that could cause adverse effects. These may include changes at the  
215 transcriptional and translational level and may be due to the insert itself or to genomic changes  
216 due to the transformation or recombination processes.

217 *Point to consider regarding the receiving environment:*

218 (e) Characteristics of the likely potential receiving environment, in particular its attributes that are  
219 relevant to potential interactions of the LMO that could lead to adverse effects (see also  
220 paragraph (g) below),<sup>39</sup> taking into account the characteristics that are components of biological  
221 diversity;

222 (f) The intended scale and duration of the environmental release.

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

225 (g) Characteristics of the LMO in relation to the receiving environment (e.g. information on  
226 phenotypic traits that are relevant for its survival in, or its potential adverse effects on the likely  
227 receiving environment – see also paragraph (e) above);

228 (h) Considerations for unmanaged and managed ecosystems (such as agricultural, forest and  
229 aquaculture systems) that are relevant for the likely potential receiving environment. These  
230 include the potential for dispersal of the LMO through, for instance, seed dispersal or  
231 outcrossing within or between species, or through transfer into habitats where the LMO may  
232 persist or proliferate;

233 (i) Potential consequences of outcrossing and flow of transgenes from an LMO to other sexually  
234 compatible species, which could lead to introgression of the transgene(s) into the population of  
235 sexually compatible species;

236 (j) Effects on non-target organisms;

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<sup>38</sup> For the purpose of this document, the term “combinatorial effects” refers to effects that may arise from the interactions between two (or more) genes. The effects may occur at the level of gene expression, or through interactions between RNA, or among gene products. The effects may be qualitative or quantitative; quantitative effects are often referred to as resulting in antagonistic, additive or synergistic effects.

<sup>39</sup> 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.

- 237 (k) Cumulative effects;<sup>40</sup>
- 238 (l) Effects of the incidental exposure of humans to (parts of) the LMO (e.g. exposure to pollen),  
239 and the toxic or allergenic effects that may ensue;
- 240 (m) Potential adverse effects as a consequence of horizontal gene transfer (HGT) of transgenic  
241 sequences from the LMO to any other organism in the likely receiving environment. With  
242 regard to HGT to micro-organisms (including viruses), particular attention may be given to  
243 cases where the LMO is also a micro-organism; and
- 244 (n) A consideration of uncertainty arising in step 1 that may significantly impact the identification  
245 of hazards in this step (see “Identification and consideration of uncertainty” under Context and  
246 scoping of the risk assessment above).

247 (*See references relevant to “[Step 1](#)”*).

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

251 *Rationale:*

252 The potential adverse effects identified in step 1 may result in risks, but this depends on the likelihood  
253 and the consequence of the effects. In order to determine and characterize the overall risk (in step 4), the  
254 likelihood of each adverse effect being realized has to be assessed and evaluated beforehand.

255 One aspect to be considered is whether the receiving environment will be exposed to the LMO in such a  
256 way that the identified adverse effects may actually occur, e.g. taking into consideration the intended use  
257 of the LMO, and the expression level, dose and environmental fate of transgene products as well as  
258 plausible pathways leading to adverse effects.

259 Other aspects to be considered here are (i) the potential of the LMO (or its derivatives resulting from  
260 outcrossing) to spread and establish beyond the receiving environment (in particular into protected  
261 areas), and whether that could result in adverse effects; and (ii) the possibility of occurrence of adverse  
262 (e.g. toxic) effects on organisms (or on organisms other than the ‘target organism’ for some types of  
263 LMOs).

264 The levels of likelihood may be expressed, for example, by the terms ‘highly likely’, ‘likely’, ‘unlikely’,  
265 ‘highly unlikely’. Parties may consider describing these terms and their uses in risk assessment  
266 guidelines published and/or adopted by them.

267 *Points to consider:*

- 268 (a) Information relating to the type and intended use of the LMO, including the scale and duration  
269 of the release, bearing in mind, as appropriate, user habits, patterns and agronomic practices;
- 270 (b) The relevant characteristics of the likely potential receiving environment that may experience or  
271 may be a factor in the occurrence of the potential adverse effects (see also step 1 (e), (f) and  
272 (g)), taking into account the variability of the environmental conditions and any long-term  
273 adverse effects. Levels of expression in the LMO and persistence and accumulation in the

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<sup>40</sup> For the purpose of this document, the term “cumulative effects” refers to effects that occur due to the presence of multiple LMOs in the receiving environment.

- 274 environment (e.g. in the food chain) of substances with potentially adverse effects newly  
275 produced by the LMO, such as insecticidal proteins, toxins and allergens;
- 276 (c) Available information on the location of the release and the receiving environment (such as  
277 geographic and biogeographic information, including, as appropriate, coordinates, information  
278 on the sexually compatible species and whether they are co-localized with the LMO and  
279 whether flowering occurs at the same time, or in general, interbreeding can occur);
- 280 (d) For the case of outcrossing and outbreeding from an LMO to sexually compatible species, the  
281 considerations would include: (i) the biology of the sexually compatible species; (ii) the  
282 potential environment where the sexually compatible species may be located; (iii) the chance of  
283 introgression of the transgene into the sexually compatible species;
- 284 (e) Expected exposure to the environment where the LMO is released and means by which  
285 incidental exposure could occur at that location or elsewhere (e.g. gene flow or incidental  
286 exposure due to losses during transport and handling);
- 287 (f) A consideration of uncertainty arising in step 2 (see “Identification and consideration of  
288 uncertainty” under “Context and scoping of the risk assessment” above).

289 (*See references relevant to “[Step 2](#)”*).

290 **Step 3: “An evaluation of the consequences should these adverse effects be realized.”**

291 *Rationale:*

292 This step describes an evaluation of the magnitude of the consequences in the likely potential receiving  
293 environment, taking into account, among others, results of tests done under different conditions such as  
294 laboratory experiments or experimental field releases. The evaluation is comparative and should be  
295 considered in the context of the adverse effects caused by the non-modified recipient or, if more  
296 appropriate, by a near-isogenic or other non-modified organism of the same species. The evaluation may  
297 also be considered in the context of the adverse effects that occur in the environment and which are  
298 associated with existing practices such as various agronomic practices, for example, for pest or weed  
299 management if such information is available and relevant. The evaluation of the consequence of adverse  
300 effects may be expressed as, for instance, ‘major’, ‘intermediate’, ‘minor’ or ‘marginal’. Parties may  
301 consider describing these terms and their uses in risk assessment guidelines published and/or adopted by  
302 them.

303 *Points to consider:*

- 304 (a) Relevant experience with the consequences of existing practices with the non-modified  
305 recipient or, if more appropriate, with a non-modified organism of the same species in the likely  
306 potential receiving environment, may be useful in order to establish baselines to evaluate, for  
307 example, the consequences of (i) agricultural practices, such as the level of inter- and intra-  
308 species gene flow, dissemination of the recipient, abundance of volunteer plants in crop  
309 rotation; occurrence of pests and/or beneficial organisms such as pollinators and pest predators;  
310 or (ii) pest management, including effects on non-target organisms in pesticide applications  
311 while following accepted agronomic practices;
- 312 (b) Adverse effects which may be direct and indirect, immediate and delayed. Some of these  
313 adverse effects may result from combinatorial and cumulative effects;
- 314 (c) Results from laboratory experiments examining, *inter alia*, dose-response relationships (e.g.,  
315 EC 50s, LD 50s) and from field trials evaluating, for instance, potential invasiveness;

316 (d) For the case of outcrossing to sexually compatible species, the possible adverse effects that may  
317 occur, after introgression, due to the expression of the transgenes in the sexually compatible  
318 species; and

319 (e) A consideration of uncertainty arising in step 3 that may significantly impact the evaluation of  
320 consequences should the adverse effects be realized (see “Identification and consideration of  
321 uncertainty” under Context and scoping of the risk assessment above).

322 (*See references relevant to “[Step 3](#)”*).

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

325 *Rationale:*

326 The purpose of this step is to determine and characterize the level of the overall risk based on the  
327 identified individual risks posed by the LMO on the conservation and sustainable use of biological  
328 diversity, taking also into account human health. The individual risks are determined on the basis of an  
329 analysis of the potential adverse effects identified in step 1, their likelihood (step 2) and consequences  
330 (step 3), and also taking into consideration any relevant uncertainty that emerged in the preceding steps.

331 It should then be determined whether the assessed risks meet the criteria set out in the protection goals,  
332 assessment endpoints and thresholds, as established in relevant legislation of the Party or in its practice.  
333 Where there is uncertainty regarding the level of risk, it may be addressed by requesting further  
334 information on the specific issues of concern or by implementing appropriate risk management strategies  
335 and/or monitoring the LMO in the receiving environment (see also step 5). Description of the risk  
336 characterization may be expressed as, for instance, ‘high’, ‘medium’, ‘low’, ‘negligible’ or  
337 ‘indeterminate due to uncertainty or lack of knowledge’. Parties may consider describing these terms and  
338 their uses in risk assessment guidelines published and/or adopted by them.

339 To date, there is no universally accepted method to estimate the overall risk but rather a number of  
340 methods are available for this purpose. The outcome of this step may be, for example, a description  
341 explaining how the estimation of the overall risk was performed.

342 *Points to consider:*

343 (a) The identified potential adverse effects (step 1);

344 (b) The assessments of likelihood (step 2);

345 (c) The evaluation of the consequences (step 3);

346 (d) Any interaction between the identified individual risks;

347 (e) Any cumulative effect due to the presence of multiple LMOs in the receiving environment; and

348 (f) A consideration of uncertainty arising in this and the previous steps (see “Identification and  
349 consideration of uncertainty” under Context and scoping of the risk assessment above).

350 (*See references relevant to “[Step 4](#)”*).

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

353 *Rationale:*

354 In this way, step 5 provides an interface between the process of risk assessment and the process of  
355 determining whether risk management measures are necessary and, if so, which measures could be  
356 implemented to manage the risks associated with the LMO.

357 The evaluation of the overall risk on the basis of the identified individual risks conducted in the previous  
358 step may lead to the conclusion that the identified risks are not acceptable in relation to the established  
359 protection goals, assessment end-points and risk thresholds, also when taking into account risks posed by  
360 the non-modified recipient and its use. Then the question arises whether risk management options can be  
361 identified that have the potential to remove the identified risks or reduce their magnitude. In the process  
362 of the formulation of risk management options, the effect of the proposed options on the identified risks  
363 should be explained. The appropriate steps of the risk assessment should then be reiterated by taking into  
364 account the implementation of the risk management options to estimate the new levels of likelihood,  
365 consequence and risk and to assess if the risk management measures are appropriate and sufficient.

366 The issues mentioned in the ‘overarching issues’ section can be taken into consideration again at the end  
367 of the risk assessment process to evaluate whether the objectives and criteria that were set out at the  
368 beginning of the risk assessment have been met.

369 The recommendation of acceptability of risk(s) should acknowledge the previously identified  
370 uncertainties. Some uncertainties may be reduced by monitoring (e.g. checking the validity of  
371 assumptions about the ecological effects of the LMO), requests for more information, or implementing  
372 the appropriate risk management options.

373 The recommendation(s) as to whether or not the risks are acceptable or manageable and  
374 recommendations for risk management options are submitted for consideration in the decision-making  
375 process.

376 *Points to consider related to the acceptability of risks:*

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

380 (b) In establishing a baseline for the comparison of the LMO, any relevant experience with the use  
381 of the non-modified recipient, and practices associated with its use in the potential receiving  
382 environment; and

383 (c) The feasibility of the adoption of risk management or monitoring strategies.

384 *Points to consider related to the risk management strategies:*

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

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

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

398 (*See references relevant to "[Step 5](#)"*).

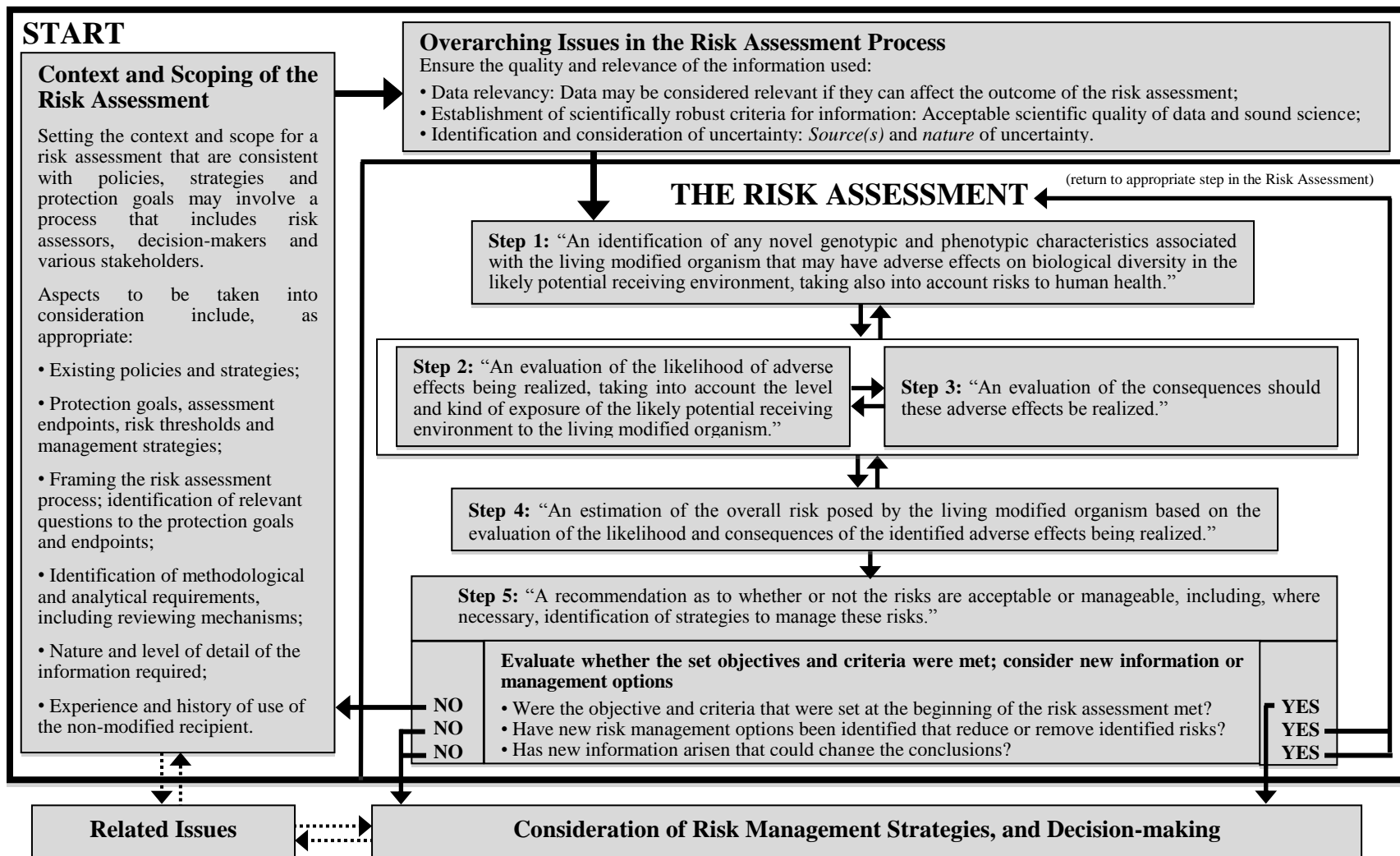
### 399 **RELATED ISSUES**

400 Some members of the AHTEG considered some issues to be related to risk assessment and decision-  
401 making process but outside the scope of this Roadmap. These issues were, *inter alia*:

- 402 • Risk management (Article 16);
- 403 • Capacity-building (Article 22);
- 404 • Public awareness and participation (Article 23);
- 405 • Socio-economic considerations (Article 26);
- 406 • Liability and redress (Article 27);
- 407 • Co-existence;
- 408 • Ethical issues.

Annex

FLOWCHART FOR RISK ASSESSMENT



**Figure 1. The Roadmap for Risk Assessment.** The flowchart represents the steps 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. The box around steps 2 and 3 shows that these steps may sometimes be considered simultaneously or in reverse order.

## PART II

### SPECIFIC TYPES OF LMOs AND TRAITS

#### A. RISK ASSESSMENT OF LIVING MODIFIED ORGANISMS WITH STACKED GENES OR TRAITS

##### 1 INTRODUCTION

2 Worldwide, a growing number of LMOs with stacked transgenic traits, particularly LM crops, are being  
3 developed for commercial uses. As a result, the number of stacked genes in a single LMO and the  
4 number of LMOs with two or more transgenic traits is growing.

5 Stacked transgenic traits can be produced through different approaches. In addition to the cross-  
6 hybridising of two LMOs, multiple trait characters can be achieved by transformation with a multigene  
7 cassette, retransformation of an LMO or simultaneous transformation with different transgene cassettes  
8 (i.e., cotransformation).

9 This guidance document focuses on stacked transgenic traits that have been produced through cross-  
10 breeding of two or more LMOs.

11 LMOs with multiple transgenic traits resulting from re-transformation, co-transformation or  
12 transformation with a multigene cassette should be assessed according to the Roadmap.

13 This guidance document complements the Roadmap for Risk Assessment developed by the AHTEG on  
14 Risk Assessment and Risk Management, and focuses on issues that are of particular relevance to the risk  
15 assessment of LMOs with stacked events generated through cross breeding of single or multiple event  
16 LMO.

17 This is intended to be a “living document” that will be shaped and improved with time as new  
18 information and/or experience becomes available and new developments in the field of applications of  
19 LMOs occur, as and when mandated by the Parties to the Protocol.

##### 20 OBJECTIVE

21 The objective of this document is to give additional guidance on the risk assessment (RA) of LMOs with  
22 stacked events generated through conventional crossing of single or multiple event LMOs. Accordingly,  
23 it is meant to complement the Roadmap for Risk Assessment<sup>41</sup> and address special aspects of LMOs with  
24 stacked transgenes/traits resulting from the conventional crossing. For the time being it will be restricted  
25 to plant LMOs.<sup>42</sup>

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<sup>41</sup> In accordance with a mandate from the Parties to the Cartagena Protocol on Biosafety (the Protocol), the AHTEG has developed ‘a “roadmap”, such as a flowchart, on the necessary steps to conduct a risk assessment in accordance with Annex III to the Protocol and, for each of these steps,’ has provided ‘examples of relevant guidance documents’. The Roadmap is presented, together with the present document, to the Parties of the Protocol on the occasion of the fifth meeting of the Conference of the Parties serving as the meeting of the Parties.

<sup>42</sup> It is also restricted to those LMO generated through the methods of Modern Biotechnology as defined in Art. 3 (i) (a) of the Protocol. LMOs derived from fusion of cells are not covered in this document.



26 **USE OF TERMS**

27 **Transformation event (TraEv)**

28 For the purpose of this document, a transformation event (TraEv) is an LM plant which results from the  
29 use of modern biotechnology applying *in vitro* nucleic acid techniques<sup>43</sup> that may involve, but is not  
30 limited to, single or multiple gene transformation cassettes. In either case, the result will be one  
31 transformation event.

32 **Stacked event (StaEv)**

33 For the purpose of this document, a stacked event (StaEv) is an LM plant generated through conventional  
34 cross breeding of two or more single parental transformation events (TraEvs) or two already stacked  
35 events. Accordingly the transgene<sup>44</sup> cassettes may be physically unlinked (i.e. located separately in the  
36 genome) and may segregate independently.

37 **Unintentional stacked event**

38 Unintentional stacked events are the result of outcrossing of stacked events into other LMOs or  
39 compatible relatives in the receiving environment. Depending on the segregation pattern of the stacked  
40 genes this may result in new and/or different combinations of TraEvs.

41 **SCOPE**

42 This guidance document focuses on stacked events (StaEv) resulting from conventional crossings  
43 between two or more single transformation events (TraEv) as parental lines so that the resulting LMO  
44 contains two or more transgenic traits. It is understood that the individual TraEvs making up the StaEv  
45 have been assessed previously in accordance with Annex III of the Cartagena Protocol on Biosafety and  
46 as described in the Roadmap.

47 **ISSUES TO BE CONSIDERED IN THE RISK ASSESSMENT**

48 **Assessment of sequence characteristics at the insertion sites and genotypic stability** (*see step 1,*  
49 *Point to consider (c) of the Roadmap for Risk Assessment*)

50 *Rationale:*

51 Although recombination, mutation and rearrangements are not limited to LMOs, the combination of  
52 transgenic traits via cross breeding may further change the molecular characteristics of the inserted  
53 genes/gene fragments at the insertion site and/or influence the regulation of the expression of the  
54 transgenes. In addition, changes to the molecular characteristics may influence the ability to detect the  
55 LMO, which may be needed in the context of risk management measures (see step 5 of the Roadmap.  
56 The reappraisal of the molecular sequence at the insertion sites, and the intactness of the transgenes may  
57 be confirmative to the molecular characteristics of the parental LMOs, but may also be a basis for  
58 assessing any intended or unintended possibly adverse effects on the conservation and sustainable use of  
59 biological diversity in the likely potential receiving environment and of potential adverse effects on  
60 human health. The extent of the reexamination may vary case by case and take into account the results of  
61 the parental LMO risk assessment.

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<sup>43</sup> See Article 3 (i) (a) of the Protocol.

<sup>44</sup> For the purpose of this document, a transgene is a nucleic acid sequence that results from the application of modern biotechnology as described in Article 3 (i) (a) of the Protocol.

62 **Assessment of potential interactions between combined events and the resulting phenotypic effects**  
 63 *(see step 1, point to consider (d) of the Roadmap for Risk Assessment)*

64 *Rationale:*

65 The combination of two or more TraEvs resulting in a StaEv may influence the expression level of each  
 66 of the transgenes and there may be interaction between the genes and the expressed products of the  
 67 different transgenes. In addition, the stacked transgenes may alter the expression of endogenous genes.

68 Therefore, in addition to information about the characteristics of the parental single-TraEv LMOs,  
 69 specific information on potential for interactions between the altered or inserted genes, stacked proteins  
 70 or modified traits and endogenous genes and their products in the StaEv LMO should be considered and  
 71 assessed. For example, it should be assessed whether the different transgenes affect the same biochemical  
 72 pathways or physiological processes, or are expected to or may have any combinatorial effects that may  
 73 result in potential for new or increased adverse effects relative to the parent LMOs.

74 **Assessment of combinatorial and cumulative effects of stacked event LMOs on the conservation**  
 75 **and sustainable use of biological diversity in the likely potential receiving environment, taking also**  
 76 **into account potential adverse effects to human health** *(see step 1, point to consider (c), step 2, point*  
 77 *to consider (c) and step 3, point to consider (b) of the Roadmap for Risk Assessment)*

78 *Rationale:*

79 Assessment of combinatorial and cumulative effects<sup>45</sup> is based on the environmental risk assessment data  
 80 for the StaEv LMO in comparison to the closely related non-modified recipient species and the parent  
 81 LMOs in the likely receiving environment, taking into consideration the results of the genotypic and  
 82 phenotypic assessments outlined above.

83 If potential new or increased adverse effects on the conservation and sustainable use of biological  
 84 diversity or on human health are identified in relation to the StaEv through the above analysis of possible  
 85 interactions, additional supporting data on StaEv may be required, such as:

- 86 (a) Phenotypic characteristics, including the levels of expression of any introduced gene  
 87 products or modified traits, compared to the parent LMOs and to relevant non-modified  
 88 recipient organisms (plants);
- 89 (b) Compositional analysis (e.g. levels of expression in the LMO and persistence and  
 90 accumulation in the environment, such as in the food chain) of substances with  
 91 potentially harmful effects newly produced by the StaEv, (e.g. insecticidal proteins,  
 92 allergens, anti-nutritional factors, etc.) in amounts that differ from those produced by the  
 93 parental LMOs or non-modified recipient organisms;
- 94 (c) Additional information depending on the nature of the combined traits. For example,  
 95 further toxicological analysis of the StaEv may be required to address any combinatorial  
 96 effects arising from the stacking of two or more insecticidal traits that result in a  
 97 broadened target range or increased toxicity.

98 Also, indirect effects due to changed agricultural management procedures, combined with the use of the  
 99 transgenic stacked event LMO, should be taken into consideration.

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<sup>45</sup> See definition of combinatorial and cumulative effects in the Roadmap (footnotes 38 and 40, respectively).

100 Intentional and unintentional StaEvs may have altered environmental impacts as a result of cumulative  
101 and combinatorial effects of the stacked traits prevalent in different LMOs of the same species in the  
102 receiving environment. Unintentional StaEvs may arise from outcrossing with other LMOs of the same  
103 species or cross-compatible relatives (see “Use of terms”). If a number of different StaEvs are cultivated  
104 in the same environment a number of varying unintentional StaEvs may occur. Changed impacts on non-  
105 target organisms or a change in the range of non-target organisms in the likely receiving environment  
106 should be taken into account.

107 **Development of specific methods for distinguishing the combined transgenes in a stacked event**  
108 **from the parental LMOs** (*see step 5, point to consider (d) of the Roadmap for Risk Assessment*)

109 *Rationale:*

110 Some of the risk management strategies for StaEvs may involve methods for the detection and  
111 identification of these LMOs in the context of environmental monitoring. Currently, many detection  
112 methods for LMOs rely on DNA-based techniques, such as polymerase chain reaction (PCR) or protein  
113 based ELISA tests targeted to single transformation events. The methods used to detect the transgene in  
114 the parental lines may not be sensitive or specific enough to differentiate between single parental  
115 transformation events and the same event being part of a stacked event. A special problem may arise  
116 particularly in the cases where the StaEv contains multiple transgenes with similar DNA sequences.  
117 Therefore, the detection of each and all individual transgenes in a StaEv may become a challenge and  
118 need special consideration.

## 119 **BIBLIOGRAPHIC REFERENCES**

120 See references relevant to the “[Guidance Document on Risk Assessment of LMOs with Stacked Genes or](#)  
121 [Traits](#)”.

## B. RISK ASSESSMENT OF LIVING MODIFIED CROPS WITH TOLERANCE TO ABIOTIC STRESS

### 1 INTRODUCTION

2 The aim of this document is to provide further guidance for the risk assessment of living modified (LM)  
3 crops with improved tolerance to abiotic stress.

4 This guidance document should be considered in the context of the Cartagena Protocol on Biosafety. The  
5 elements of Articles 15 Annex III of the Protocol also apply to LM crops with tolerance to abiotic stress.  
6 Accordingly, the methodology and points to consider<sup>46</sup> contained in Annex III are also applicable to this  
7 type of LMO.

8 The potential environmental adverse effects of an LM crop with abiotic stress tolerance depends on (i)  
9 the receiving environment; (ii) the modified crop, (iii) phenotypic changes resulting from the genotypic  
10 changes made to the plant and (iv) its intended use. A risk assessment would be performed on a case-by-  
11 case basis in accordance with Annex III of the Protocol.

12 This guidance document complements the Roadmap for Risk Assessment developed by the AHTEG on  
13 Risk Assessment and Risk Management, and focuses on issues that are of particular relevance to the risk  
14 assessment of LM crops tolerant to abiotic stress.

### 15 USE OF TERMS

16 “Abiotic stresses” are environmental conditions caused by non-living factors that are detrimental or  
17 suboptimal to the growth, development and/or reproduction of a living organism. Types of abiotic  
18 stresses include, for example, drought, salinity, cold, heat, soil pollution and air pollution (e.g., nitrous  
19 oxides, ozone).

### 20 RISK ASSESSMENT

21 While the same general principles used in the risk assessments of other types of LMOs also apply to LM  
22 crops with increased tolerance to abiotic stress, there are a number of specific issues that may be of  
23 particular importance when assessing the risks of LM crops tolerant to abiotic stresses.

24 Questions that may be relevant to the risk assessment of LM crops with tolerance to abiotic stress in  
25 connection with the intended use and receiving environment include:

- 26 • Would the tolerance trait have the potential to increase the invasiveness, persistence or  
27 weediness of the LM crop that causes adverse effects to other organisms?
- 28 • Would a LM plant expressing tolerance to a particular abiotic stress have other advantages in  
29 the targeted receiving environment that cause adverse effects?
- 30 • Would any LMO arising from outcrossing with the abiotic stress tolerant LM crop, have the  
31 potential to colonize an ecosystem beyond the targeted receiving environment?
- 32 • Would the abiotic stress tolerance trait, for example, via pleiotropic effects, have the potential to  
33 affect, *inter alia*, pest and disease resistance mechanisms of the LM crop?

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<sup>46</sup> Paragraphs 8 and 9 of Annex III, respectively.

34 Some of the potential adverse effects to be evaluated in the risk assessment, from the introduction of  
35 crops tolerant to abiotic stress into the environment include, for example: a) increased selective  
36 advantage(s) other than the intended tolerance trait; b) increased persistence in agricultural areas and  
37 increased invasiveness in natural habitats; c) adverse effects on organisms exposed to the crop; and d)  
38 consequences of potential gene flow to wild or conventional relatives. While these adverse effects may  
39 exist regardless of whether the tolerant crop is a product of modern biotechnology or conventional  
40 breeding, some specific issues may be more relevant in the case of abiotic stress tolerant LM crops.

41 **Characterization of the LM crop with tolerance to abiotic stress in comparison with its non-**  
42 **modified crop** (*see step 1 of the Roadmap for Risk Assessment*)

43 *Rationale:*

44 The first step in the risk assessment process involves the characterization of genotypic or phenotypic,  
45 biological, intended and unintended changes associated with the abiotic stress tolerant LM crop that may  
46 have adverse effects on biodiversity in the likely receiving environment, taking into account risks to  
47 human health. This step is the ‘hazard identification step’ in other risk assessment guidance.

48 The identification of genotypic and phenotypic changes in the abiotic stress tolerant LM crop, either  
49 intended or unintended, is typically done in comparison with the non-modified recipient organism (see  
50 step 1 of the Roadmap). The non-modified comparator provides the baseline information for comparison  
51 of trials when it is grown at the same time and location as the LM crop. Comparisons with the observed  
52 range of changes in the non-modified crop in different environments, also provides baseline information.

53 *Challenges with respect to experimental design:* Abiotic stress crops may present unique challenges in  
54 experimental design for risk assessment. In some cases, for instance, an approach uses different  
55 reference plant lines, which typically include a range of genotypes representative of the natural variation  
56 in the crop species. In such conditions, choosing appropriate comparators could be a challenge and there  
57 are several proposals on whether and how the comparative approach can be used to characterize LM  
58 crops tolerant to abiotic stress in these likely receiving environments. Another important consideration is  
59 whether the experimental design properly controlled for the effect of the abiotic stress trait. In the  
60 extreme case, when the non-modified crop has never been grown in the range of conditions of the  
61 receiving environment because the abiotic stress conditions prevent or severely affect the growth of the  
62 non-modified crop, a comparative approach between the LM crop and the non-modified crop will need to  
63 be adjusted.

64 The use of non-isogenic reference lines can make it more difficult to identify statistically meaningful  
65 differences. In some situations when a comparator may not be available to carry out a meaningful  
66 comparison, a characterization of the abiotic stress tolerant LM crop as a novel genotype in the receiving  
67 environment may be conducted. In the future, information available from “omics” technologies, for  
68 example, “transcriptomics” and “metabolomics”, if available, may help to detect phenotypes (e.g., the  
69 production of a novel allergen or anti-nutrient) that cannot be detected using a comparison between field  
70 grown plants at a suboptimal condition.

71

72 *Points to consider:*

- 73 (a) Characteristics of the LM crop under the abiotic stress and non-stress conditions and under  
74 different stresses, if applicable;
- 75 (b) Likelihood of gene flow to wild or domestic relatives; and
- 76 (c) Whether one or more suitable comparators are available and the possibility of their use in the  
77 appropriate experimental design.

78 **Unintended characteristics** (*see step 1 of the Roadmap for Risk Assessment*)79 *Rationale:*

80 Both intended and unintended changes to the LM crop which are directly or indirectly associated with the  
81 abiotic stress tolerance that may have adverse effects should be identified. These include changes to the  
82 biology of the crop plant (e.g. if the genes alter multiple characteristics of the plant) or to its distribution  
83 range in relation to the potential receiving environment (e.g. if the plant can grow where it has not grown  
84 before), that may cause adverse effects.

85 The abiotic-stress-tolerant LM crop may have unintended characteristics such as tolerances to other types  
86 of biotic and abiotic stresses, which could lead to a selective advantage of these crop plants under  
87 conditions other than that related to the modified trait. For instance, crops modified to become tolerant to  
88 drought or salinity may be able to compete better than their counterparts at lower and higher growing  
89 temperatures.

90 It is also possible the LM crops with enhanced tolerance to an abiotic stress could have changes in seed  
91 dormancy, viability, and/or germination rates under other types of stresses. Particularly if genes involved  
92 in abiotic stress are also involved in crucial steps in physiology, modifications involving these genes  
93 may, therefore, have pleiotropic effects. Such LM crops may also transfer genes for stress tolerance at  
94 higher frequencies than observed in non-modified crops.

95 A potential mechanism for interactions between abiotic and biotic stresses may exist in plants. For  
96 example, drought or salinity-tolerant LM crops may acquire a changed tolerance to biotic stresses, which  
97 could result in changed interactions with their predators, parasitoids and pathogens, and, therefore, have  
98 both direct and indirect effects on organisms that interact with them.

99 *Points to consider:*

- 100 (a) Any intended or unintended change that may lead to selective advantage or disadvantage  
101 acquired by the LM crop under other abiotic or biotic stress conditions that could cause  
102 adverse effects;
- 103 (b) Any change in the resistance to biotic stresses and how these could affect the population of  
104 organisms interacting with the LM crop; and
- 105 (c) A change in the substances (e.g., toxin, allergen, or nutrient profile) of the LM crop that could  
106 cause adverse effects.

107 **Increased persistency in agricultural areas and invasiveness of natural habitats** (*see steps 1, 3 and 5  
108 of the Roadmap for Risk Assessment*)

109 *Rationale:*

110 Climate change, water depletion or elevated salt content are examples of factors that limit the growth,  
111 productivity, spread or persistence of a crop. Expression of the genes for abiotic stress tolerance could  
112 result in increased persistence of the modified crop in agricultural areas. Expression of these genes may  
113 also alter the capacity of LM crops to spread to and establish in climatic and geographic zones beyond  
114 those initially considered as the likely or potential receiving environments.

115 The gene(s) inserted for tolerance to, for instance, drought and salinity might also affect molecular  
116 response mechanisms to other forms of abiotic stress, such as cold temperatures. For example, when the  
117 genetic modification affects genes that also regulate key processes in seeds, such as abscisic acid (ABA)  
118 metabolism, physiological characteristics such as dormancy and accumulation of storage lipids may also  
119 be changed. In such cases, the seeds of a tolerant crop, modified for drought or salinity tolerance, may  
120 acquire in addition tolerance to cold resulting in an increased winter survivability of the seeds. Therefore,  
121 an abiotic stress-tolerant crop may acquire the potential to persist better than its conventional counterpart  
122 under different abiotic-stress conditions.

123 *Points to consider:*

- 124 (a) Consequences of the increased potential for persistency of the modified crop in agricultural  
125 habitats and consequences of increased potential for invasiveness in natural habitats;
- 126 (b) Need for control measures if the abiotic stress-tolerant crop shows a higher potential for  
127 persistency in agricultural or natural habitats, that could cause adverse effects;
- 128 (c) Characteristics that are generally associated with weediness such as prolonged seed dormancy,  
129 long persistence of seeds in the soil, germination under a broad range of environmental  
130 conditions, rapid vegetative growth, short lifecycle, very high seed output, high seed dispersal  
131 and long-distance seed dispersal; and
- 132 (d) Effects of climate change on agriculture and biodiversity and how this could change the habitat  
133 range of the LM crop in comparison to the non modified crop.
- 134 (e) If the LM crop expressing tolerance, would have a change in its agriculture practices.

135 **BIBLIOGRAPHIC REFERENCES**

136 *See references relevant to the “[Guidance Document on Risk Assessment of LM Crops with Tolerance to](#)*  
137 *[Abiotic Stress](#)”.*

## C. RISK ASSESSMENT OF LIVING MODIFIED MOSQUITOES

### 1 INTRODUCTION

2 Living modified (LM) mosquitoes are being developed through modern biotechnology to reduce  
3 transmission of vector borne human pathogens, particularly those that cause malaria, dengue and  
4 chikungunya. Control, including eradication of such diseases, is a recognized public health goal. Some of  
5 the strategies being developed are to control mosquito vectors by suppressing their population or  
6 reducing their competence. These strategies can be subcategorized according to the technology involved  
7 and the method used. Some are intended to develop LM mosquitoes that are genetically modified to be  
8 sterile or self-limiting (i.e., unable to pass the modified trait on indefinitely through subsequent  
9 generations). Modern biotechnology techniques for developing sterile LM mosquitoes are different from  
10 those based on the use of irradiation to induce male sterility.

11 Other modern biotechnology strategies are also being used for developing LM mosquito populations that  
12 are self-sustaining or self-propagating (i.e., heritable modifications intended to spread through the target  
13 population). The strategy used is an important factor to be considered in the risk assessment and risk  
14 management process since there might be different points to be considered, depending on the specific  
15 strategy used.

16 The biology and ecology of mosquitoes on the one hand, and their impact on public health as vectors of  
17 human and animal diseases on the other hand, pose new considerations and challenges during the risk  
18 assessment process, which have mainly dealt with LM crop plants thus far.

19 This guidance document provides information for the risk assessment of environmental releases of LM  
20 mosquitoes and aims at helping to conduct risk assessments for environmental releases of LM  
21 mosquitoes. Although the focus of this guidance is on LM mosquitoes, in principle, it may also be useful  
22 for the risk assessment of similar non-LM mosquito strategies.

23 The main emphasis of this guidance document is the assessment of potential risks to biodiversity.  
24 Nevertheless, the potential adverse effects to human health arising from environmental releases of LM  
25 mosquitoes should also be considered.

26 This guidance document complements the Roadmap for Risk Assessment developed by the AHTEG on  
27 Risk Assessment and Risk Management and focuses on specific issues that may need special  
28 consideration on the risk assessment for environmental releases of LM mosquitoes.

### 29 OBJECTIVE

30 The objective of this document is to give additional guidance on the risk assessment (RA) of LM  
31 mosquitoes in accordance with Annex III to the Cartagena Protocol on Biosafety.<sup>47</sup> Accordingly, it aims  
32 at complementing the Roadmap for Risk Assessment on specific issues that may need special  
33 consideration for the environmental release of LM mosquitoes.

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<sup>47</sup> The Parties to the Cartagena Protocol on Biosafety have mandated the AHTEG to 'develop a "roadmap", such as a flowchart, on the necessary steps to conduct a risk assessment in accordance with Annex III to the Protocol and, for each of these steps, provide examples of relevant guidance documents'. The Roadmap is meant to provide reasoned guidance on how, in practice, to apply the necessary steps for environmental risk assessment as set out in Annex III of the Protocol. The Roadmap also demonstrates how these steps are interlinked.



34 **SCOPE**

35 This document focuses on the specific aspects of risk assessment of LM mosquitoes developed to be  
36 used in the control of human and zoonotic diseases such as malaria, dengue, chikungunya, yellow fever  
37 and West Nile.

38 **ISSUES TO BE CONSIDERED IN THE RISK ASSESSMENT**

39 *(See step 1 of the Roadmap for Risk Assessment of LMOs)*

40 Specific and comprehensive considerations should be undertaken with respect to the potential adverse  
41 effects of a particular LM mosquito, taking into account the species of the mosquito, the LM trait, the  
42 intended receiving environment, and the objective and scale of the intended release. These considerations  
43 should focus on, for instance: (a) description of the genetic modification; (b) the kinds of possible  
44 adverse effects for which there are scientifically plausible scenarios; (c) the species and ecological  
45 processes that could be affected by the introduction of the LM mosquitoes; (d) the protection goals of the  
46 country where the LM mosquitoes will be introduced; and (e) a conceptual link between the identified  
47 protection goals and the introduction of the LM mosquito into the environment.

48 The biology and, to some extent, the ecology of the mosquito species that transmit malaria and dengue  
49 are well known in many regions of the world. However, in certain regions and in the environment where  
50 the LM mosquito is likely to be released, more information may be needed depending on the nature and  
51 scale of the LM strategy to be deployed. In many of these environments few studies have been conducted  
52 to examine gene flow among vectors, their mating behaviour, the interactions between vectors sharing  
53 one habitat, how pathogens respond to the introduction of new vectors, etc. Such information may be  
54 needed to establish a baseline in order to successfully assess the risks of LM mosquitoes. Additionally,  
55 methods for the identification of specific ecological or environmental hazards are also needed.

56 **Effects on biological diversity (species, habitats, ecosystems, and ecosystem services)**

57 *(See step 2 of the Roadmap for Risk Assessment of LMOs)*

58 *Rationale:*

59 The release of LM mosquitoes may have a negative impact on the target vector and pathogen<sup>48</sup> and other  
60 species, such as:

61 *New or more vigorous pests, especially those that have adverse effects on human health:* (i) the released  
62 LM mosquitoes may not function as expected, for example gene silencing or production failures could  
63 result in the release of non-sterile or competent mosquitoes and thus increase the vector population or  
64 disease transmission; (ii) the released LM mosquitoes could transmit another disease more efficiently  
65 than indigenous non-LM mosquitoes, such diseases might include yellow fever, chikungunya, etc.; (iii)  
66 suppression of the target mosquito might result in the population of another vector species to increase  
67 and result in higher levels of the target disease or the development of a new disease in humans and/or  
68 animals. These other vector species may include other mosquito vectors of other diseases; (iv) the  
69 released LM mosquitoes might become pests; (v) the released LM mosquitoes might cause other pests to  
70 become more serious, including agricultural pests and other pests that affect human activities.

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<sup>48</sup> For the purpose of this guidance, the term “target vector” refers to the mosquito that transmits the disease and “target pathogen” is the disease causing agent transmitted by the target mosquito.

71 *Harm to or loss of other species:* The released LM mosquitoes might cause other species (for instance  
72 fish that rely seasonally on mosquitoes for food) to become less abundant. These include species of  
73 ecological, economic, cultural and/or social importance such as wild food, endangered, keystone, iconic  
74 and other relevant wildlife species. Ecological effects might result from competitive release if the target  
75 mosquito population is reduced or from trophic consequences of species that rely on mosquitoes for food  
76 at specific times of the year. Effects may also occur if (i) the target mosquitoes transmit a disease to  
77 animal species, (ii) the released LM mosquitoes transmit a disease to animal species more efficiently,  
78 (iii) another vector of an animal disease was released from control when the target mosquito population  
79 was reduced, or (iv) the population of a target pathogen is reduced or lost and this may affect other  
80 organisms that interact with it.

81 Although mosquitoes, like other insects, typically have strong reproductive isolating mechanisms that  
82 will not allow interspecific gene flow, if sterile interspecific mating between released LM mosquitoes  
83 and other mosquito species should occur, it could disrupt the population dynamics of these other species,  
84 leading to harm or loss of valued ecological species. Moreover, cessation of transmission of pathogens to  
85 other animals (e.g., West Nile virus to birds, Rift Valley fever virus to African mammals) might alter the  
86 population dynamics of those species, favouring increases in their numbers.

87 *Disruption of ecological communities and ecosystem processes:* The ecological communities in the  
88 ephemeral, small aquatic habitats occupied by the non-LM mosquitoes are unlikely to be disrupted  
89 beyond the possibilities already addressed above under “harm to or loss of other species.” However, if  
90 the released LM mosquitoes were to inhabit natural habitats (e.g. tree-holes), disruption of the associated  
91 community is a possibility. The released LM mosquitoes might degrade some valued ecosystem process.  
92 This might include processes such as pollination or support of normal ecosystem functioning. These  
93 processes are often referred to as “ecosystem services”. However, the valued ecosystem processes may  
94 also be culturally or socially specific. Under some circumstances, mosquito species are significant  
95 pollinators. In those cases, mosquito control of any kind might reduce the rate of pollination of some  
96 plant species or cause a shift to different kinds of pollinators. Habitats in which mosquitoes are the  
97 dominant insect fauna (e.g., high Arctic tundra, tree holes) would be changed if mosquitoes were  
98 eliminated; however, the common target vector species are usually associated with human activity and  
99 therefore not as closely tied to ecosystem services.

100 *Points to consider:*

- 101 (a) Impacts on the target mosquitoes and pathogens resulting from the use of the strategy under  
102 consideration;
- 103 (b) Whether the LM mosquitoes have the potential of causing adverse effects on other species  
104 which will result in the other species becoming agricultural, aquacultural, public health or  
105 environmental pests, or nuisance or health hazards;
- 106 (c) Whether the target mosquito species is native or invasive to a given area;
- 107 (d) The habitat range of the target mosquito species and whether the habitat range is likely to be  
108 affected by climate change;
- 109 (e) Any other species (e.g. animal hosts, larval pathogens or predators of mosquitoes) in addition to  
110 the pathogen, that typically interact with the LM mosquito in the likely receiving environment;
- 111 (f) Whether the release of LM mosquitoes is likely to affect other mosquito species that are  
112 pollinators or otherwise known to be beneficial to ecosystem processes;
- 113 (g) Whether the LM mosquitoes are likely to have an adverse effect on other interacting organisms,  
114 e.g. predators of mosquitoes;

- 115 (h) Whether species replacement by other disease vector species may occur, and if so, whether it  
116 can result in an increased incidence of the target disease or new diseases in humans or animals.

117 **Gene Flow**

118 (See steps 2 and 3 of the Roadmap for Risk Assessment of LMOs)

119 *Rationale:*

120 With regard to the biosafety of LM mosquitoes, gene flow refers to the transfer of transgenes<sup>49</sup> or genetic  
121 elements from the LM mosquitoes to non-LM mosquitoes. It can occur via cross-fertilisation or other  
122 movement of the transgenes or genetic elements. Various factors may influence gene flow and any  
123 associated adverse effects, such as, the strategy, the transgenes, the gene drive system<sup>50</sup> and the stability  
124 of the trait(s) carried by the mosquito over generations, as well as the receiving environment, etc.

125 *Gene flow through cross-fertilization:* Some LM mosquitoes are being developed to spread the  
126 introduced trait rapidly through the target mosquito population. For instance, when introduced into  
127 *Anopheles gambiae*, the trait may be expected to spread throughout the *A. gambiae* species complex.  
128 Other LM mosquito technologies are designed to be self-limiting and, in such cases, spread of the  
129 transgenes or genetic elements in the target mosquito population is not intended or expected. For the self-  
130 limiting technologies, the potential for an unexpected spread of the introduced trait should be considered  
131 by focusing on the assumption that any management strategy to limit the spread could fail. Gene flow  
132 between different species should be considered for all of the LM mosquito technologies in spite of the  
133 fact that mosquitoes, like other insects, typically have strong reproductive isolating mechanisms that will  
134 not allow interspecific gene flow. Identifying the key reproductive isolating mechanisms and possible  
135 conditions that could lead to the breakdown of such mechanisms is of particular importance in the risk  
136 assessment of LM mosquitoes with this trait. In addition, the fitness conferred by the introduced trait and  
137 the population size and frequency of the introduction of the LM mosquito into the environment will also  
138 determine the likelihood and rate of spread of the transgenes or genetic elements.

139 *Horizontal gene flow:* For the purpose of this document, “horizontal gene flow”, is the movement of  
140 genetic information from one organism to another through means other than sexual transmission. Gene  
141 drive systems for moving genes into wild populations may be the initial focus of the risk assessment. The  
142 risk of horizontal gene flow in LM mosquitoes that do not contain a gene drive system is likely to be  
143 smaller but should nevertheless be assessed on a case-by-case basis.

144 *Persistence of the transgene in the environment.* Some of the transgenes in LM mosquitoes are designed  
145 not to persist whereas others are expected to spread rapidly and/or persist through wild populations. In  
146 cases where the LM mosquitoes have been found through the risk assessment process to have the  
147 potential to cause adverse effects to the biological diversity, taking also into account human health,  
148 methods to reduce the persistence of the transgene in the environment needs to be considered

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<sup>49</sup> For the purpose of this document, a transgene is a nucleic acid sequence in an LMO that results from the application of modern biotechnology as described in Article 3 (i) a of the Protocol.

<sup>50</sup> Gene drive systems are methods of effectively introducing the desired gene into a mosquito population (Selfish DNA versus Vector-Borne Disease, Environmental Health Perspectives (2008) 116 - <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2235231/pdf/ehp0116-a00066.pdf> ).

149 *Points to consider:*

- 150 (a) Whether LM mosquitoes have the potential to transfer the modified traits to wild mosquito  
151 populations (when it is not an intended strategy) and/or to non-related organisms, and if so, the  
152 occurrence of any potential undesirable consequences;
- 153 (b) Whether the LM mosquitoes have the potential to induce undesirable characteristics, functions,  
154 or behaviour within the target mosquito species, other wild related species or non-related  
155 organisms;
- 156 (c) Any undesirable consequence should the transgene persist in the environment.

157 **Evolutionary responses (especially in target mosquito vectors or pathogens of humans and**  
158 **animals)**159 *(See step 1 of the Roadmap for Risk Assessment of LMOs)*160 *Rationale:*

161 Any strong ecological effect also exerts an evolutionary selection pressure on the human and animal  
162 pathogens and the mosquito vectors. The main evolutionary effects are those that could result in a  
163 breakdown in the effectiveness of the technology and the resumption of previous disease levels. Some  
164 LM mosquito strategies aim at modifying the mosquito vector's ability to transmit diseases through  
165 changes in its physiological mechanisms. An evolutionary effect resulting in the development of  
166 resistance to physiological mechanisms in the targeted pathogen might occur when modifying mosquito  
167 vector competence. This might harm the effectiveness of the strategy used and result in a population of  
168 pathogens that may be transmitted more easily by all types of vectors.

169 Other evolutionary effects could be hypothesized, including effects resulting from climate change, but  
170 they would first require the occurrence of some adverse effect on a species, community or ecosystem  
171 effect. Therefore, consideration of secondary evolutionary effects can be postponed until such effects are  
172 identified and found to be significant.

173 *Points to consider:*

- 174 (a) Whether the target mosquito vector has the potential to evolve and avoid population  
175 suppression, regain vector competence or acquire new or enhanced competence to another  
176 disease agent, and if so, the occurrence of any possible undesirable consequences;
- 177 (b) Whether the trait has the potential to evolve and thus lose its effectiveness, or the pathogen to  
178 evolve and overcome the limitation posed by the genetic modification, and if so, the occurrence  
179 of any possible undesirable consequences.

180 **RISK-MANAGEMENT STRATEGIES**181 *(See step 5 of the Roadmap for Risk Assessment of LMOs)*

182 Risk assessors may want to consider risk-management strategies such as the quality control of the  
183 released LM mosquitoes and monitoring them and the environment for potential unintended adverse  
184 effects. There should also be strategies in place for halting the release and application of mitigation  
185 methods if an unanticipated effect occurs. Careful implementation of the technology including the  
186 availability of mitigations measures (such as an alternative set of control measures should a problem  
187 occur) and the integration of other population control methods should be considered. In some

188 circumstances methods to reduce the persistence of the transgene in the environment or to mitigate  
189 adverse effects resulting from the expression of the transgene might be needed. Monitoring during and  
190 after the environmental release of the LM mosquitoes so as to address prompt detection of unexpected  
191 adverse effects may also be considered.

192 *Points to consider:*

193 (a) Availability of monitoring methods to:

194 (i) Measure the efficacy and effectiveness of LM mosquito technology;

195 (ii) Assess the potential evolutionary breakdown of the LM mosquito technology (monitoring  
196 for transgene stability and proper function over time);

197 (iii) Determine the level to which the identified adverse effects may be realized, including  
198 detection of unexpected and undesirable spread of the transgenic trait (monitor for  
199 undesirable functions or behaviours within target species and other wild related species).

200 (b) Availability of mechanisms to recall the LM mosquitoes and transgenes in case they spread  
201 unexpectedly (e.g. mass release of wild-type mosquitoes above a certain threshold, alternative  
202 control methods including genetic control).

203 (c) Availability of methods for managing the dispersal of the LM mosquitoes and ensuring that they  
204 do not establish themselves beyond the intended receiving environment (eg. vegetation-free  
205 zones, traps, high threshold gene drive systems).

206 (d) Availability of methods to manage potential development of resistance, e.g. in the target vector  
207 or pathogen.

## 208 **OTHER ISSUES**

209 There are other factors that may be taken into consideration in the decision for environmental releases of  
210 LM mosquitoes which are not covered by Annex III of the Protocol. They encompass, *inter alia*, social,  
211 economic, cultural and health issues associated with the application and acceptance of the technology.

## 212 **BIBLIOGRAPHIC REFERENCES**

213 See references relevant to the "[\*Guidance Document on Risk Assessment of LM Mosquitoes\*](#)".

*Annex IV***RECOMMENDATIONS TO THE CONFERENCE OF THE PARTIES SERVING AS THE MEETING OF THE PARTIES TO THE CARTAGENA PROTOCOL ON BIOSAFETY AT ITS FIFTH MEETING**

1. The Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management took note of the deliberations under the Open-ended Online Expert Forum on Risk Assessment and Risk Management in particular about the need for further guidance on specific aspects of risk assessment and considered the existing guidance materials on risk assessment of living modified organisms.
2. The AHTEG recognized the importance of involving experts in the various scientific and technical fields relevant to risk assessment in any future activity taking into account the limited financial and human resources.
3. The following recommendations were made by the AHTEG:
  - (a) The document “Guidance on Risk Assessment of Living Modified Organisms” should be published and distributed, including an online version under the Biosafety Clearing-House (BCH), in all UN languages;
  - (b) The “Guidance on Risk Assessment of Living Modified Organisms” should be further tested for example during regional workshops including cooperation with existing initiatives for capacity-building and training, as appropriate;
  - (c) The “Guidance on Risk Assessment of Living Modified Organisms” should be revisited within two years and the need for an update of the list of background materials should be assessed within a year;
  - (d) Further development of guidance on risk assessment of living modified organisms should be considered. The topics identified and prioritized during the first meeting of the AHTEG as well as those mentioned at the second meeting could be the starting point for the further development of guidance on risk assessment (see list annexed hereto as annex V);
  - (e) A process should be established for the incorporation of background materials, available in the Biosafety Information Resources Centre of the Biosafety Clearing-House, that are relevant in the different sections of the “Guidance on Risk Assessment of Living Modified Organisms”. In order to assist this process, the Secretariat should be requested to revise the common format for submission of records to the Biosafety Information Resources Centre (BIRC) of the BCH with the view to identifying and including a mechanism to link BIRC records on risk assessment to specific sections of the guidance document;
  - (f) Recognizing that the exchange of information is a central element for identifying living modified organisms or specific traits that have been assessed as having the potential to cause adverse effects on the conservation and sustainable use of biological diversity taking also into account risks to human health, a process should be established by:
    - (i) Urging Parties and inviting non-Parties to submit relevant information to the BCH on experiences in conducting risk assessment with regard to this topic;

- (ii) Requesting the Secretariat to undertake a regular analysis of the information contained in the BCH within the context of this process and reporting to the COP-MOP for that purpose;
- (iii) Organizing workshops where the information submitted would be analyzed through a guided-process.

(g) The goals of the above recommendations (a) to (f) could be achieved by a combination of an extended Open-ended Online Expert Forum on Risk Assessment and Risk Management and an AHTEG on Risk Assessment and Risk Management, as well as a combination of online conferences, ad hoc discussion groups and face-to-face meetings with a view to:

- (i) Developing additional guidance documents on the basis of the “Guidance on Risk Assessment of Living Modified Organisms” on specific types of living modified organisms and traits;
- (ii) Reviewing the text of the “Guidance on Risk Assessment of Living Modified Organisms” and updating the lists of background materials;
- (iii) Incorporating background materials, available in the Biosafety Information Resources Centre of the Biosafety Clearing-House, that are relevant to the different sections of the “Guidance on Risk Assessment of Living Modified Organisms”;
- (iv) Analysing the results of the workshops on living modified organisms or specific traits that have been assessed as having the potential to cause adverse effects.

(h) Human and financial resource implications should be considered for the process set up to achieve the above goals.

*Annex V*

**TOPICS FOR THE DEVELOPMENT OF GUIDANCE MATERIALS ON RISK ASSESSMENT**

*Further topics indentified in the first meeting of the AHTEG as priorities for the development of guidance:*<sup>51</sup>

- Post-release monitoring and long-term effects of LMOs released into the environment;
- Risk assessment and risk management in specific receiving environments;
- Risk assessment of living modified microorganisms and viruses;
- Risk assessment of living modified pharmaplants;
- Risk assessment of living modified crops;
- Risk assessment of living modified trees;
- Risk assessment of living modified fish;
- Risk assessment living modified organisms for production of pharmaceutical and industrial products;
- “Co-existence” between LMOs and non-LMOs in the context of small scale farming;
- Risk assessment of living modified plants for biofuels;
- Risk assessment of living modified organisms produced through synthetic biology.

*Further topics identified in the second meeting of the AHTEG as possible priorities for the development of guidance:*

- Uncertainty analysis;
- Establishment of criteria for transparency and reproducibility of information;
- Interface between risk assessment and risk management;
- Environmental risk assessment and monitoring taking into account human health;
- Unintentional transboundary movements;
- Risk assessment and management of LMOs intended for introduction into unmanaged environments.

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<sup>51</sup> From annex II of the report of the first meeting of the Ad Hoc Technical Expert Group on Risk Assessment and Risk Management (UNEP/CBD/BS/COP-MOP/5/INF/13).