SUBMISSION FROM THE NETHERLANDS (PARTY)

REVIEW OF THE GUIDANCE ON RISK ASSESSMENT OF LIVING MODIFIED ORGANISMS BY THE NETHERLANDS FOCAL POINT

FORM FOR THE SCIENTIFIC REVIEW OF THE GUIDANCE ON RISK ASSESSMENT OF LIVING MODIFIED ORGANISMS

The completed review forms are to be mailed to the Secretariat at: riskassessment.forum@cbd.int . Reviews from Parties and other Governments are to be submitted by their National Focal Points. Reviews from organizations are to be submitted through their head offices.

Dear colleagues,

We are very happy that you have offered the possibility for a scientific review of the Guidance on risk assessment of living modified organisms, as requested by COPMOP-5, and we are sending you our comments in the proposed format.

Our comments are based on a review done by the Netherlands Advisory Committee on Genetic Modification[1]. The Committee has indicated that the time for performing the review was very short, and that it has only been able to do a review on main issues of the document. Detailed comments are therefore lacking, but we are sure that they can be filled in during subsequent rounds of discussion in the internet forum and during the activities of the AHTEG.

In COPMOP-5 it has become clear that the guidance is much appreciated, especially by countries with less experience in environmental risk assessment of LMOs. On the other hand, it was also clear that a thorough scientific review of the document is necessary. We therefore think that efforts to further improve the quality of the document in the AHTEG process are very worthwhile and necessary. Our comments should be seen as a token of our commitment to the AHTEG process, and to the improvement of the scientific quality of the document.

We are very grateful for all the work and effort that the SCBD and the AHTEG have invested in the document, and we hope that you will be able to continue the work in the same spirit.

Best wishes, and good luck,

Inge van der Leij
Ministry of Infrastructure and the Environment
Netherlands Focal Point for the Cartagena Protocol on Biosafety

[1] http://www.cogem.net/main-adviesdetail-home.aspx?pageid=13&loc=2&version=&mode=&id=590

i. Reviewer's information

*Please select **only one** of options below*

This scientific review of the Guidance on Risk Assessment of Living Modified Organisms is being submitted on behalf of a:

☒ Party. Please specify: The Netherlands

☐ Other Government. Please specify: <Country's name>

☐ Organization: Please specify: <Organization's name>

ii. Overall evaluation

*Please select **only one** answer for each section*

Q1. How do you evaluate the level of consistency of the following sections of the Guidance with the Cartagena Protocol on Biosafety, particularly with its Article 15 and Annex III?

	Very poor	Poor	Neutral	Good	Very good
• Roadmap for risk assessment	☐	☐	☐	☒	☐
• Risk assessment of living modified organisms with stacked genes or traits	☐	☐	☐	☒	☐
• Risk assessment of living modified crops with tolerance to abiotic stress	☐	☐	☐	☒	☐
• Risk assessment of living modified mosquitoes	☐	☐	☐	☒	☐

Q2. How do you evaluate the usefulness of the following sections of the Guidance as tools for assisting countries in conducting and reviewing risk assessments of LMOs in a scientifically sound and case-by-case manner?

	Very poor	Poor	Neutral	Good	Very good
• Roadmap for risk assessment	☐	☐	☐	☒	☐
• Risk assessment of living modified organisms with stacked genes or traits	☐	☐	☐	☒	☐
• Risk assessment of living modified crops with tolerance to abiotic stress	☐	☐	☐	☒	☐
• Risk assessment of living modified mosquitoes	☐	☐	☐	☒	☐

Q3. How do you evaluate the usefulness of the following sections of the Guidance as tools for assisting countries in conducting and reviewing risk assessments of LMOs introduced into various receiving environments?

	Very poor	Poor	Neutral	Good	Very good
• Roadmap for risk assessment	☐	☐	☐	☒	☐
• Risk assessment of living modified organisms with stacked genes or traits	☐	☐	☐	☒	☐
• Risk assessment of living modified crops with tolerance to abiotic stress	☐	☐	☐	☒	☐
• Risk assessment of living modified mosquitoes	☐	☐	☐	☒	☐

Q4. How do you evaluate the usefulness of the "Roadmap" as a tool for assisting countries in conducting and reviewing risk assessments of LMOs of different taxa?

	Very poor	Poor	Neutral	Good	Very good
• Roadmap for risk assessment	☐	☒	☐	☐	☐

ADDITIONAL COMMENTS ON THE OVERALL EVALUATION

Please add any additional comment you may have regarding the overall evaluation of the first version of the "Guidance on Risk Assessment of Living Modified Organisms" below.

Q5. Roadmap: the scores for Q 1-3 are 'good', but still, many improvements are needed, as indicated in the section-by-section review. As such, the document is 'good', but not 'good enough'.
The document 'poor' as a Roadmap for all types of LMOs. The general framework is of course valid in general, because Annex III, that is the basis of the document, is applicable to all types of LMOs. But the detailed explanations in the document are mostly only applicable to LM crops.

The documents on stacked genes, abiotic stress and LM mosquitoes also score 'good', but, like the Roadmap, also these documents need improvement, as we indicate below.

iii. Section-by-section review

*Please select **only one** of the boxes for each question*

PART I: THE ROADMAP FOR RISK ASSESSMENT

1. INTRODUCTION

Q6. Are all the concepts in this section relevant and accurate from a scientific point of view?

☐ Yes

☒ No. Please comment:

The concept accep tof 'comparative risk assessment' in the paragraph 'Risk assessment is done in a comparative manner …' needs further explanation. An important concept is that the

	nature of the appropriate comparator fully depends on the nature and the scope of the risk assessment question that is asked. The examples that follow in the text of the paragraph present a rather fragmented picture instead of a reasoned approach.
Q7. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: The definition of a transgene is not consistent throughout the document. On page 3 a transgene is defined as “a nucleic acid sequence in an LMO that results from the application of modern biotechnology” (footnote 11), i.e., a gene that is present in an organism that has been constructed using modern biotechnology. According to page 15 a transgene is “a nucleic acid sequence that results from the application of modern biotechnology” (footnote 23). The first definition would appear to be more 'product-driven', while the second definition would be 'process-driven'. The second definition would also imply that a gene constructed by means of modern biotechnology is already a transgene before it has been introduced into an organism. The same definition should be used throughout the document. Although the roadmap is meant to give guidance on the risk assessment process for all types of LMOs this aim is not met. This is reflected in the terminology used and in the aspects that are included in the roadmap. As the terminology in the roadmap is not appropriate for all types of LMOs and because not all aspects are included that are relevant for the risk assessment of other types of LMOs, the use of this roadmap for other types of LMOs, such as viruses and bacteria, is limited. For instance, the aspects that are relevant for determining the risk of living modified micro-organisms such as the host range of the wild type micro-organism or the occurrence of shedding (excretion of living modified micro-organisms), which are of key importance for some applications of micro-organisms, are not mentioned at all. We suggest to develop more guidance documents for different types of living modified organisms, such as micro-organisms (including viruses), fish and insects. It is stated that the roadmap applies to all types of LMOs and products thereof (footnote 4 page 1). This suggests that the roadmap also applies to products that no longer contain living modified organisms. Here the Roadmap follows the terminology of the Cartagena Protocol, and we realize that the expression refers to products that contain living modified organisms. However, this expression could be misinterpreted, and, as the roadmap is developed to be used in capacity building activities, we suggest that it should be clarified that the roadmap only applies to those products that still contain living modified organisms.
Q8. Are all the concepts in this section expressed in a language that could be easily understood by the target users?	☐ Yes ☒ No. Please comment: The introduction mentions a large number of issues that would need to be clarified by providing examples. For instance, a statement is made that the data should be of an acceptable scientific quality. A number of abstract criteria follow in the text. There is, however, no further guidance presented on these issues and no examples are given of relevant or irrelevant

	data or of data that are scientifically acceptable or unacceptable. In addition a number of aspects are listed that should be taken into consideration when setting the context and scope for a risk assessment. The aspects that are mentioned are amongst others protection goals, assessment end-points, risk thresholds, management strategies and methodological and analytical requirements. The document provides no guidance on the process of identification of specific protection goals, assessment endpoints and risk thresholds or on the identification of methodological and analytical requirements. It is the task of the Competent Authority of the Party to determine these criteria. The above mentioned aspects play a crucial role in the risk assessment process and therefore guidance on the determination of these aspects should be incorporated in the document. Also in other places the documents lacks guidance. The description of the risk assessment process, for instance, is general and does not provide illustrations of the various concepts. More detailed explanations and examples could be given in an annex to the guidance document or in accompanying documents. These should be clearly identifiable as examples of specific issues in the risk assessment approach. These documents could be offered in the list of background material, with a clear identification of the specific isasue for which they offer further guidance and explanation. We think that the list of background materials is of the utmost importance, amnd should be further improved. This could be a way to better organize the list of background materials, while also reducing the number of documents. It could complicate the question of how the list should be managed, but we trust that the AHTEG will be able to make proposals for this issue.

2. THE RISK ASSESSMENT

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

Q9. Are all the concepts in this section relevant and accurate from a scientific point of view?	☒ Yes ☐ No. Please comment: <Type here>
Q10. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: Throughout the document more attention should be paid to the intended use of the LMO, e.g., for cultivation vs. for import and processing. In our risk assessment practice this difference in intended use is of major importance for the considerations chosen in the risk assessment. In general, more guidance should be given in the text on those cases where information is necessary for the risk assessment and on the cases where this information is not needed ('nice-to-know' vs. 'need-to-know'). For instance, when no cultivation occurs, assessment of the potential adverse effects on non-target organisms is less relevant.

Q11. Are all the concepts in this section expressed in a language that could be easily understood by the target users?	☐ Yes ☒ No. Please comment: An important concept in Step 1 and elsewhere in the Roadmap is the identifiction of characteristics of the LMO that 'may have adverse effects' on the environment. The term adverse effects can be interpreted broadly. Although it is mentioned that scientifically plausible scenarios should be identified in step 1 (page 6), it is not clear who determines whether scenarios are scientifically plausible or based on what criteria they can be considered scientifically plausible. Therefore, the inclusion of scenarios that are not scientifically plausible in the risk assessment process remains possible. The inclusion of criteria for the scientific plausibility of a scenario would reduce the likelihood that non-scientific scenarios are accidentally included in the risk assessment process. It is mentioned, notably in Points to consider 1 c, molecular characterization, that the relevance and availability of the information may vary. While this is true, and goes for many points mentioned in step 1 and elsewhere in the Roadmap, it is also not helpful, if no criteria are provided to decide when information is or is not relevant.
Step 2: "An evaluation of the likelihood of adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the living modified organism"	
Q12. Are all the concepts in this section relevant and accurate from a scientific point of view?	☒ Yes ☐ No. Please comment: <Type here>
Q13. Does this section include all the necessary relevant concepts?	☒ Yes ☐ No. Please comment: <Type here>
Q14. Are all the concepts in this section expressed in a language that could be easily understood by the target users?	☒ Yes ☐ No. Please comment: <Type here>
Step 3: "An evaluation of the consequences should these adverse effects be realized"	
Q15. Are all the concepts in this section relevant and accurate from a scientific point of view?	☐ Yes ☒ No. Please comment: Point to consider c): 'Results from laboratory experiments examining, inter alia, dose-response relationships (e.g., EC 50s, LD 50s) and from field trials evaluating, for instance, potential invasiveness.' This is a good example of a text that would need much more explanation in order to be clear. The effect of an LM crop on non-target organisms should only be assessed if there is an indication that expression of a transgene could adversely affect non-target organisms. EC50 or LD50 values are used to establish the toxicity of a substance and reflect the concentration that produces a response in 50% of the test population (EC50) or the dose that is lethal to 50% of the test population (LD50). Studies on EC 50 and LD 50 are usually presented in the context of the evaluation of population growth of non-target organisms. Lethal effects are important in this respect. But also sub-lethal effects can have a large

	influence on populations of non-target organisms, and the assessment of sub-lethal effects on non-target organisms should be part of the assessment of the effect of an LM crop on non-target organisms. Therefore, the assessment of sub-lethal effects, as well as lethal effects, should be mentioned explicitly in the guidance document, in the context of determining effects on population growth of non-target organisms.
Q16. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: An important factor in the determination of the magnitude of a risk is the (ir)reversibility of the potential adverse effects, and this should be taken into considferation carefully. An effect that could be irreversible is for instance the transfer of a transgene to wild relatives by outcrossing. The (ir)reversibility of potential effects should be taken into consideration carefully. It should be mentioned in this step, as well as in step 4.
Q17. Are all the concepts in this section expressed in a language that could be easily understood by the target users?	☐ Yes ☒ No. Please comment: See comments to Q15 and 16

Step 4: "An estimation of the overall risk posed by the living modified organism based on the evaluation of the likelihood and consequences of the identified adverse effects being realized"	
Q18. Are all the concepts in this section relevant and accurate from a scientific point of view?	☒ Yes ☐ No. Please comment:
Q19. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: In step 4 the level of overall risk of an LMO is determined and characterized. In the guidance it is mentioned that when there is uncertainty regarding the level of risk, this uncertainty may be addressed by requesting further information, by implementing appropriate risk management strategies and/or monitoring the LMO in the receiving environment (page 10). We are of the opinion that monitoring is indeed a helpful tool to detect unexpected adverse effects of an LMO and we stress the importance of monitoring in dealing with uncertainty. The concept of monitoring should therefroe receive more attention in the guidance document.
Q20. Are all the concepts in this section expressed in a language that could be easily understood by the target users?	☐ Yes ☒ No. Please comment: Point to consider e: 'Any cumulative effect due to the presence of multiple LMOs in the receiving environment': More guidance is needed on the concept of cumulative effects. The concept is also mentioned in the guidance on stacked genes: 'Intentional and unintentional StaEvs may have altered environmental impacts as a result of cumulative and combinatorial effects of the stacked traits prevalent in different LMOs of the same species in the receiving environment.' Explanations are needed about the different situations where cumulative effects are thought to occur, and how they should be evaluated. Also, the difference between cumulative and combinatorial effects needs to be clarified throughout the documents. We are not sure that these terms have been used consistently throughout the documents.
Step 5: "A recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage these risks"	
Q21. Are all the concepts in this section relevant and accurate from a scientific point of view?	☐ Yes ☒ No. Please comment: In step 5 a clear distinction should be made between the questions of manageability and acceptability of risks. Manageability of a risk is an aspect that belongs, in part, to risk assessment, but acceptability of a risk is decided on by the competent authority, in the decision making stage, and does not belong to risk assessment. Still, the expertise of risk assessors is helpful or sometimes even necessary to determine the magnitude and (ir)reversibility of the consequences of a risk, in the context of protection goals. The Roadmap therefore should clarify the precise role of the risk

	assessor in the risk assessment-risk management process. The Roadmap could also point out that information on the possible benefits of an LMO could be important when evaluating the acceptability.
Q22. Does this section include all the necessary relevant concepts?	☒ Yes ☐ No. Please comment: <Type here>
Q23. Are all the concepts in this section expressed in a language that could be easily understood by the target users?	☐ Yes ☒ No. Please comment: See comments to Q21
3. RELATED ISSUES	
Q24. Does the "Related Issues" section include all relevant issues related to risk assessment and decision-making process but that are outside the scope of the Roadmap?	☐ Yes ☒ No. Please comment: The roadmap lists a number issues that are related to risk assessment and the decision making process but which are considered to be outside the scope of the roadmap (e.g. co-existence, risk management, public awareness). One of the listed issues is 'risk management', which is confusing since a major part of the considerations in step 5 of the risk assessment process refers to risk management measures.
4. FLOWCHART	
Q25. Does the flowchart provide an accurate graphic representation of the risk assessment process as described in the Roadmap?	☐ Yes ☒ No. Please comment: Step 5 mentions that it should be checked whether the objective and criteria set at the beginning of the risk assessment process were met, but a determination of objectives and criteria is not mentioned as such at the beginning of the process.

PART II: SPECIFIC TYPES OF LMOs AND TRAITS	
A. RISK ASSESSMENT OF LIVING MODIFIED ORGANISMS WITH STACKED GENES OR TRAITS	
Q26. Are all the concepts in this section relevant and accurate from a scientific point of view?	☐ Yes ☒ No. Please comment: The process of risk assessment that is described seems to be straightforward. It is however important to realize that the assessment of potential interactions and effects from stacked events and their gene products could be very complex and verey difficult to solve. For the final conclusion on the eventual risks of an LMO the overall effect of the LMO is the important feature that should be assessed. In the statement that 'indirect effects due to changed agricultural management procedures, combined with the use of the transgenic stacked event LMO, should be taken into consideration'. It is not clear to what extent this should be done. 'Agricultural management procedures' could refer to many different aspect. Adverse effects originating from agricultural management procedures that are not a direct effect of the LM character of a crop should not be part of the risk assessment. Also, these considerations would not be specific for LM crops with stacked genes. Therefore they should be part of the Roadmap, and do not have to be repeated in the document on stacked genes.
Q27. Does this section include all the necessary relevant concepts?	☒ Yes ☐ No. Please comment:
Q28. Are all the concepts in this section expressed in a language that could be easily understood by the target users?	☐ Yes ☒ No. Please comment: See comments to Q26
B. RISK ASSESSMENT OF LIVING MODIFIED CROPS WITH TOLERANCE TO ABIOTIC STRESS	
Q29. Are all the concepts in this section relevant and accurate from a scientific point of view?	☒ Yes ☐ No. Please comment: <Type here>
Q30. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: This guidance document mentions that the chracterization of the LM crop in step 1 could be a challenge, as the nonmodified grop may never have been grown in the receiving environment. The approach may therefore need to be adjusted. How the approach should or could be adjusted is not mentioned. This aspect should receive more attention, preferably by making suggestion how adjustments could be made. The characterization of the LM crop may be based on a theoretical considerations rather than on a real-life comparative approach.
Q31. Are all the concepts in this section expressed in a language that could be easily understood by the target users?	☐ Yes ☒ No. Please comment: See comment to Q30

C. RISK ASSESSMENT OF LIVING MODIFIED MOSQUITOES

Q32. Are all the concepts in this section relevant and accurate from a scientific point of view?	☒ Yes ☐ No. Please comment: <Type here>
Q33. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: The document focuses on adverse effects that the LM mosquito may have on the environment, but should also take into account the adverse effect of the trait on the mosquito itself, e.g., on its fitness, lifespan and/or developmental rate. The biology of the non-modified mosquito could be altered by the introduced trait, and this could affect the potential risk of the LM mosquito. This should be taken into account in the risk assessment. It should be mentioned that the LM mosquito could affect the ecology if the host range of the LM mosquito is altered compared to the non-modified mosquito. This aspect could be mentioned as a potential effect of the LM mosquito on ecology, but also as a potential effect on biodiversity. Also, the potential effect on the ecosystem of diminishing the incidence of disease should be mentioned. Changes in disease incidence could directly or indirectly affect ecology and biodiversity by affecting the occurrence of host organisms as well as other organisms. These considerations also include the effects of disease incidence in man as a host, and as a consequence, on the occurrence of man in specific environments, and the impact that might result from this. Gene flow is one of the issues that should be considered in the risk assessment. In the paragraph on 'gene flow through cross-fertilization' it is mentioned that that the likelyhood and rate of spread of the trangenes or genetic elements is (amongst others) determined by the fitness conferred by the introduced trait (page 25). This probably refers to the effect of the introduced trait on the insect in the relevant receiving environment. Therefore, the sentence should be changed in order to reflect that the fitness (dis)advantage of the trait on the LM mosquito affects the rate of spread of the transgenes. In the paragraph on rtisk management strategies (step 5) one of the point to consider is the availability of mechanisms to recall the LM mosquitoes and transgenes if they spread unexpectedly. We seriously doubt whether mechanisms that could be used to recall LM mosquitoes are available; therefore the suggestion that a recall would be possible could better not be made.
Q34. Are all the concepts in this section expressed in a language that could be easily understood by the target users?	☐ Yes ☒ No. Please comment: See comment to Q33

ADDITIONAL COMMENTS ON THE SECTION-BY-SECTION REVIEW

Please add any additional comment you may have regarding particular sections of the first version of the "Guidance on Risk Assessment of Living Modified Organisms" below.

Q35. A major problem with the guidance documents appears to be that they are quite ambitious, and that the drafting has apparently taken many discussions. This necessarily shows in the quality of the document. We are sure that, when the document is scrutinized in detail, a number of inconsistencies will turn up. The time available for reviewing the document has not been enough for us to perform such a critical appraisal. In the AHTEG process, time should be found to improve the general quality of the document.
