SUBMISSION FROM THE CENTER FOR ENVIRONMENTAL RISK ASSESSMENT (ORGANIZATION)

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

The Guidance for Risk Assessment of Living Modified Organisms (the "Guidance") was developed through collaborative efforts between the Open-ended Online Expert Forum and the Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management.*

The aim of the Guidance is to further elaborate the methodology for risk assessment of living modified organisms (LMOs) in accordance with the Cartagena Protocol on Biosafety, and in particular in accordance with Annex III of the Protocol.

The Guidance is intended to be a "living document" that will be improved with time as new experience becomes available and new developments occur in the field of applications of LMOs, as and when mandated by the Parties to the Cartagena Protocol on Biosafety.

At the fifth meeting of the Conference of the Parties serving as the meeting of the Parties to the Protocol (COP-MOP), the Parties to the Protocol welcomed the first version of the Guidance and noted that it requires further scientific review and testing to establish its overall utility and applicability to living modified organisms of different taxa introduced into various environments.

The Executive Secretary was therefore requested to coordinate a review process of this first version of the Guidance among Parties and other Governments, through their technical and scientific experts, and relevant organizations.

The following questions are aimed at seeking views to assist the Open-ended Online Expert Forum and the AHTEG in revising the Guidance.

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.

* Additional information on the development of the "Guidance on Risk Assessment of Living Modified Organisms" may be found in document UNEP/CBD/BS/COP-MOP/5/12 (see "Official Documents" at http://www.cbd.int/doc/?meeting=MOP-05).

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: <Country's name>

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

☒ Organization: Please specify: Center for Environmental Risk Assessment (CERA), ILSI Research Foundation

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 <u>introduced into various receiving environments</u>?					
	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 "<u>Roadmap</u>" as a tool for assisting countries in conducting and reviewing risk assessments of LMOs <u>of different taxa</u>?					
	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. *The largest flaw in the guidance documents relates to their failure to support case by case risk assessment, and their failure to add value beyond the text that is already available in Annex III. In some ways, this simply points out the elegance of Annex III in describing the risk assessment process.*

iii. Section-by-section review

*<u>Please select **only one** of the boxes for each question</u>*

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: Although it is certainly important in the overall context of the Protocol, the Precautionary Approach is not a risk assessment concept - it is a decision making concept. A scientific risk assessment cannot be precautionary - it is simply an assesment of risk. The way that Uncertainty is presented here is misleading and does not accurately reflect how uncertainty is dealt with in real risk assessment (for LMOs or otherwise). The Roadmap appears to recommend that every step of an assessmnet needs

	to include an extensive analysis of uncertainty in all of its forms, as well as an uncertainty analysis of each step in combination. If this were actually to be carried out the analysis of uncertainty would far eclipse the risk assessment in size. Consideration of uncertainty in risk assessment is not an academic pursuit. In any scientific statement, uncertainties can be identified related to data variability, sources of error etc. However, the vast majority of these uncertainties will be insignificant for a risk assessment. A risk assessment does not need to address and identify ALL potential sources of uncertainty. Rather, it must identify SIGNIFICANT uncertainties which have the potential to affect the results of the assessment. This is not a minor distinction in practice. The text included in the Roadmap is counterproductive in helping risk assessors identify significant sources of uncertainty, instead encouraging them to expend energy providing a detailed uncertainty analysis for uncertainties which will largely be meaningless for the final assessment
Q7. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: In its characterization of risk assessment, the Introduction fails to acknowledge that while risk assessment is a scientific pursuit, it is not an academic endeavor. A risk assessor is not seeking to characterize risk in order to expand human knowledge, but rather to inform necessary decision or action by the government. This leads to an inordinate focus on minor details while failing to acknowledge that one of the principle challenges of producing a good risk assessment is focusing on the most crucial information for determining risk - rather than searching for the most complete set of data that can be assemb led.
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 language used in the roadmap is both highly sophisticated and finely parsed. Simple, understandaple concepts from Annex III are expanded in such a way as to make them more confusing, rather than more clear. Although there are many true statements included in the introduction, the way the introduction is structured and the way the information is presented does not provide a coherent explanation of what a risk assessment is and why it should be conducted. As one example, the context and scoping of the risk assessment is discussed in the final section of the introduction, following both a discussion of "overarching" considerations and of uncertainty. It is impossible to think of analyzing the uncertainty related to your assessment without first having an understanding of the context and scope. This section should be first, not last.
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: The roadmap is here moving away from "case by case" risk assessment and trying to elaborate general guidance without having a specific case. This is very

	difficult to do and one of the challenges is trying to identify what information will be relevant. In doing this, it takes simple descriptions from Annex III, and loses much of the context by trying to generalize a list of relevant characteristics without considereing any particular organism or any particular receiving environment. So for example, in the "points to consider regarding the characterization of the LMO" section a. provides a list of characteristics that are "relevant" to characterize for the LMO including "iv. ecological function, and v. as a component of biological diversity that is important for the conservation and sustainable use of biological diversity in the context of Article 7(a) and Annex I of the Convention. For the vast majority of LMOs that have been introduced to date (GE crops for agriculture), these two characteristics will be irrelevant. Further, the roadmap identifies these characteristics without providing any context as to how one might go about characterizing them. Where is an example of a characterization of any organism "as a component of biological diversity that is important for the conservation and sustainable use of the biological diversity in the context of Article 7(a) and Annex I of the Convention?" In section (c) of the Points to Consider, relating to molecular characterization there is also a list of characteristics which are unlikely to be relevant to most risk assessments. For example, while it is true that changes in expression of endogenous genes due to the effects of a transgene are possible, and that these changes could theoretically result in an adverse effect - the roadmap fails to offer any context as to how this issue is addressed in a practical risk assessment. It is neither necessary nor practical to require an expression level analysis for every endogenous gene in order to verify that the expression level is unchanged in the LMO or that any changes do not produce adverse effects. Instead, most risk assessments identify characteristics that are important for the LMO and its interactions with the environment (for example known toxins, or reproductive capacity) and use phenotypic analyses to ensure that the LMO does not have altered characteristics in this regard. Another clear example is in point (m) on horizontal gene transfer. HGT is not a widespread phenomenon of relevance to most LMO risk assessments. In the last 15 years of experience with the introduction of LMOs, and associated risk assessments, there is little evidence to support the inclusion of HGTas a broadly applicable point of interaction between the LMO and its environment. This is a subject of concern only under extraoridnary circumstances.
Q10. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: It would be very difficult to develop a generic list of concepts for this section that would cover every LMO in every receiving environment.
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: Once again, the language used her is technically sophisticated and very academic. The way each subject is treated appears to be designed to maximize the complexity of the considerations rather than simplify them for practical risk assessment.

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: Once again, this section appears to be primarily concerned with identifying a large number of characteristics rather than identifying a set that would be broadly relevant. For example, in the Points to consider (b) the coordinates of a release are only likely to be relevant to very small releases (such as a field trial) or where an actual risk has been identified that is related to a particular location. Also, the persisence and accumulation of substances in the environment will only be relevant in a particular subset of risk assessments where the LMO produces a substance that is known to have an adverse impact. In (f) the consideration of uncertainty is again being elevated. There will always be some uncertainty related to exposure, and the likelihood of adverse consequences but in most cases the level of uncertainty will not have an impact on the conclusions of the assessemnt.
Q13. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: Although exposure is mentioned as a consideration for establishing likelihood, the Roadmap fails to point out that exposure is absolutely necessary for the realization of adverse effects. If evidence suggests that exposure will be negligible or zero, then the likelihood of adverse effects will also approach zero.
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: See comments from previous sections
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: See Points to consider (b) "Adverse effects which may be direct and indirect, immediate and delayed. Some of these adverse effects may result from combinatorial and cumulative effects;" This point is misplaced. The purpose of this step is to evaluate the consequence of an identified adverse effect. This point does nothing to evaluate consequences but appears instead to be urging assessors to go back and identify additional adverse effects. Nowhere are examples provide which identify what a combinatorial or cumulative effect is, or explain what the impact on consequences of such an effect might be.
Q16. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: Once again, the structure of the Roadmap is working against its utility here. What we have is a list of things that might be considered - each being relevant for only a small subset of actual cases. There is also a failure to make the necessary link to the scope/context of the risk

	assessment. Consequences should be considered in the context of identified protection goals.
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 on previous sections

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: There aren't many concepts presented here so it is difficult to answer "yes or no." It is not easy to see how the text in this section is going to help anyone conduct a risk assessment. Points to consider (e) is not scientifically valid. LMOs in the receiving environment are part of the receiving environment and should be considered in that context. It is not clear what about the presence of other LMOs needs particular consideration for cumulative effects. This is not trivial, as it implies that there is somehow a common characteristic of LMOs, regardless of their individual identity, that is important to consider for cumulative risk but that cannot be specifically identified. This is very contrary to the principles of a science based risk assessment.
Q19. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment:
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: <Type here>
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: Once again, while there are many true statements in this section, the way they are organized and presented gives a fals impression of the complexity of reaching a conclusion in risk assessment. There is very litte vaue added to what is already included in Annex III. Once again the consideration of uncertainty can be singled out for failing to provide the context that uncertainties need to be significant, and potentially impact the conclusions of the assessment in order to be discussed. It is not necessary to reduce uncertainties that are inconsequential for the assessment.
Q22. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment:
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 above comments
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: We could identify hundreds of issues that are "related to risk assessment, but outside the scope of the Roadmap." A more pertinent question is why would we want

	to? This sections serves no clear purpose in helping risk assessors conduct risk assessment.
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: The flowchart is not perfect, and in particular step 5 is overly complex. Having said that, as a tool for providing guidance to risk assessors trying to complete an assessment, the flowchart by itself is more usful than the accompanying text.

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 "Assessment of sequence characteristics at the insertion site and genotypic stability" implies that sequence data must be generated to complete a risk assessment of a plant with a stacked trait. This is not the case. Further, there is no added value to a risk assessor reading this section beyond what is already included in Annex III The "Assessment of combinatorial or cumulative effects.." section does not provide any useful information on how to conduct an assessment in a practical context. It simply seems to add a lengthy list of required data and analyses that are not dictated by Annex III, are unlikely to be related to the scope and context of a risk assessment and will not be helpful in assessing risk The detection of stacked events is entirely a risk management consideration, and it is inappropriately discussed here - implying that somehow difficulty in distinguishing between stacked events and single events with the same molecular basis presents a risk in and of itself. This is not the case.
Q27. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: There is no scientifically credible guidance in this section that would help an assessor determine when and if additional analysis would be necessary for a stacked trait compared to a single gene insertion. All of the available scientific experience and data suggests that the kind of genomic and or cumulative/synergistic interactions that are being described in this document are highly unlikely and require very special circumstances to arise. Instead of detailing a list of additional analyses that might be required, a more useful approach to take for this document would be to produce some guidance for assessors on how to identify when such interactions are likely to occure (i.e. when two introduced genes have similar functions or interact in a common chemical pathway).
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: The vocabulary in this section, particularly the acronyms used to describe stacked events are not in common usage.
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: This section has a better grounding in science than the previous two, and is generally more useful as a tool for considering risk assessment. One sentence in the introduction suggests that abiotic stress tolerance conferred

	through modern biotechnology may present additional environmental risks compared to abiotic stress tolerance conferred through other methods of plant breeding. This is unsupported by available science. There is also one section - "Characterization of the LM crop with tolerance to abiotic stress in comparison with it's non-modified crop" that could use some review for scientific validity. The section points out that the stress tolerance trait itself might affect the collection of data for comparative analysis due to the difference in response of the plants to abiotic stress. This certainly may be true, but the section fails to relate this back to risk assessment. It is important to keep in mind that the purpose of collecting this data is ultimately to assess risk, not to academically identify all possible differences between a LM plant and its progenitor. The recommendation of "omics" technologies for characterizing the LM plant in stress conditions is difficult to justify scientifically - and should be mentioned in the context of other methodolgies for characterizing enviornmental risk.
Q30. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: Overall, this section does a better job of highlighting issues that are relevant for consideration in risk assessment of plants with abiotic stress tolerance, without simply providing an overwhelming list of potential characteristics or considerations. One concept that is missing is discussion of the "cost" of abiotic stress tolerance. Most tolerance traits can be expected to have a metabolic cost associated with them - usually an energy cost which may impact the potential for the plant to persist under conditions of low selection pressure (i.e. low abiotic stress). This can have a significant impact on the assessment of a plant's potential to survive and persist in an environment over time and it is important to understand that abiotic stress tolerance is unlikely to simply be a "free" or wholly advantageous trait. Otherwise, there are some scientifically valid concepts (i.e. gene flow to wild relatives) that are not necessarily of more importance for abiotic stress tolerance traits than other traits.
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: This section stands out from the previous two in this area. The language used to present abiotic stress tolerance and how it is relevant for environmental risk assessment is quite useful. Particularly, the first page including the introduction and a very nice set of questions framing the risk assessment. Some of this breaks down as the points are elaborated, and the document delves into areas that are not unique to abiotic stress tolerant crops.
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:

Q33. Does this section include all the necessary relevant concepts?	☐ Yes ☐ No. Please comment:
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: .

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. *The members of the AHTEG have clearly put a lot of time and effort into preparing and negotiationg these guidance documents. Certainly their commitment should be applauded. Unfortunately, the resulting guidance is flawed and ultimately does not serve as a useful companion to Annex III.*

Much of this can be contributed to either a lack of clarity as to the purpose of the guidance document, or to differing views among the AHTEG members as to what was needed. The result is a lengthy, generally unhelpful listing of concepts and "points to consider" that have very limited real world application.

It is also worth pointing out that, since Annex III was finalized in 2000, there has been a decade of additional real world experience with conducting environmental risk assessment for LMOs. Essentially none of this experience is reflected in the guidance documents.