SUBMISSION FROM THE UK STATUTORY ADVISORY COMMITTEE ON RELEASES TO THE ENVIRONMENT (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: <UK statutory Advisory Committee on Releases to the Environment >

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. *In general, the focus of the guidance tends too much towards identifying issues that could be considered in risk asessments without linking these to specific risk hypotheses. More emphasis is needed on the process of risk assessment, including but not limited to that laid out in the flowchart e.g. the use of tiered approaches.Otherwise, the guidance may lead to disproportion and a non-evidenced based approach that will not aid in decision making.*

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:
Q7. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: The use of worst case scenarios can be a useful tool in risk assessment. For example, in considering the consequences of a trait from the LMO being transferred to other organisms by horizontal gene transfer. Tiered approaches

may be helpful in characterising risks e.g.in determining whether beneficial organisms in the same taxonomic Order as the pest targeted by an insecticidal LM plant could be adversely affected.

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: We are not convinced that those with little experience in risk assessment will understand what is meant by assessment endpoints and risk thresholds. These terms are not used in Annex III. Examples would help.

The first sentence in paragraph 3: Annex III does not refer to unintended effects and their mention here does not explain their significance to risk assessors. For example, it would be useful to explain that unintended effects can be divided into 2 categories i.e. those that can be foreseen and those that are geninuinely unanticipated and if / how these categories can be dealt with in risk assessments.

The flowchart refers to determing risk thresholds in the context of scoping the RA - this is missing in the paragraph that deals with identifying assessment endpoints. It would be useful if the guidance explained when it is important to define a level of change in a particular variable that can be taken as conferring an unacceptable risk to biological diversity (taking into account human health). Otherwise, data on biodiversity in particular are likely to show differences that do not have any meaning for decision-makers.

The reference to the key steps in RA and their possible relevance to each other is vague. The guidance should refer to the flowchart and make sure these relationshipis are clear in the sections dealing with the particular steps - this is not the case at present (see below).

It is helpful that the guidance points out that the provision of additional information does not necessarily help to reduce uncertainty and can make decision-making more difficult. However, this statement needs to be linked to other bullet points i.e. (i) the importance of framing the risk hypothesis accurately so that the data generated answer the question (i.e. meet the criteria for relevancy). (ii) In some cases it might be that the nature of the uncertainty means that it can't be addressed through the provision of more data in the risk assessment but may need to be dealt with by monitoring or possibly risk management.

Bullet point 4 on page 5 states that less information may be available - this is not relevant. It's the nature and level of detail of information that is required, which is relevant and amongst other things, this will depend on the biology/ecology of the reciepient organism and the scale of environmental exposure e.g. whether its for import only, field testing or commercial cultivation.

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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:
Q10. Does this section include all the necessary relevant concepts?	☒ Yes ☐ No. Please comment: <Type here>
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: The points to consider in (a) are not helpful without examples or rephrasing e.g. changes in the non-modified recipient's taxonomic relationships and changes in its centres of origin that could lead to adverse effects. Points to consider in (c) would also be more helpful with examples. The text explains that the availability and relevance of information may vary but it is not clear where/ how particular information may be useful in hazard identification e.g. data on levels of expression and stability. Similarly in (d) it would be useful to include an example of where data on transcript levels (rather than changes at the translational level) would be useful in hazard identification. Without these types of examples the guidance lacks a sense of proportion and does not encourage a strategic use of information that facilitates decision-making. It is important to emphasise the need to define an adverse effect as far as possible and a casual link between a characteristic of the LMO and this effect or the next steps will generate information that will not help in decision-making.
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: It would be useful to emphasise a systematic approach to problem formulation i.e. relate this step to step 1 and explain why steps 2 and 3 should be considered in parallel.
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:
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: >
Q16. Does this section include all the necessary relevant concepts?	☒ Yes ☐ No. Please comment: <It is important to recognise that steps 2 and 3 are carried out in parallel because it will not be necessary to consider likelihood/ exposure any any detail if no adverse consequences have been identified (e.g. through

	geneflow) and vice versa. As discussed above it is important to link this step to step 1. At present, the distinction between steps 1 and 3 is not clear when reading the 'points to consider' in the respective steps.
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: >
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: <Type here>
Q19. Does this section include all the necessary relevant concepts?	☒ Yes ☐ No. Please comment: <Type here>
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: <Type here>
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: <>
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: Are the risk management strategies referred to in decision-making the same as those referred to in step 5?
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: <Type here>

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: Insertion sites and genotypic stability: There is no a priori reason to expect, or evidence to suggest, that crossing parental GMOs will lead to changes in the molecular characteristics of the GM events in the hybrids. Should this occur, it is likely to lead to loss of the traits. Such a genetic change is no more likely to occur than between genes in non-GMOs, and selective breeding will mean that defective traits will be selected against. It is of course possible to confirm the nature of the GM event at the molecular level by PCR-based diagnostic tests. These can be carried out if there is a concern that the traits are altered, but need not be carried out routinely if the traits are phenotypically stable in the hybrid. Potential interactions between combined events: The combination of two or more TraEvs in a StaEv is only likely to influence expression levels of the transgenes or of endogenous genes if they show significant levels of sequence homology (in the promoters or coding regions). This can be anticipated, and at worst will lead to the loss or reduction in strength of the phenotypic trait, due to post-transcriptional gene silencing. It is sensible to consider evidence about whether stacked transgenes might have interactions at the protein level (eg have functions in related pathways that may lead to synergistic effects in the stacked GMO), but in the absence of such evidence the hybrids can be considered to have additive, rather than synergistic properties. It is not proportionate to carry out detailed compositional, toxicological etc. analyses on stacked GMOs in the absence of evidence that would indicate synergistic (as opposed to additive) phenotypes in the hybrids. The analysis of parental types will provide relevant information on composition, toxicology etc., that will allow a rational assessment of the effects of stacking on human health and the environment. Additional such analyses on the stacked GMOs is not expected to add new information in comparison with analyses of the parental lines, while adding significantly to the cost of notifications.
Q27. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: <Type here>
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: <Type here>

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: Many of the points to consider in this additional guidance are applicable to the risk assessment of LM plants more generally. It would be much more helpful if this chapter dealt with specific issues associated with LM crops tolerant to abiotic stress taking an evidence- based approach i.e. using the scientific literature to identify plausible risk scenarios. The final statement in the section on risk assessment states that there may be some specific issues that are more relevant to tolerant LM crops than those produced by conventional breeding but does not elaborate (and it needs to). In the section on comparison with non-modified crops the text states that the use of non-isogenic reference lines can make it more difficult to identify statistically meaningful differences ; we note that stress tends to vary across trial sites, which must also be taken into account if field trials are required to address a specific risk hypothesis. The development of LM crops with tolerance to abiotic stress(es) may allow for the cultivation of these plants in a natural environment. The increase in the area of land for food production will inevitably be harmful to the natural environment. This will be an important factor in contexting the risk assessment.
Q30. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: <Type here>
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: <Type here>
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: The document is perfunctory and fails to provide adequate details on the risk assessment or management of LM mosquitoes. Primary literature sources have been taken out of context and/or poorly understood (e.g., Benedict et al. 2008). A tiered approach to testing of LM mosquitoes must be emphasised in this sort of guidance. While the guidelines draw the distinction between self-limiting and self-sustaining technologies this seems to be disregarded in the rationale provided. Self limiting strategies (the type of strains currently under field trials) Loss of other species/disruption of ecological communities. The guidance fails to draw on the substantial ecological information about the role of mosquitoes in natural communities. It provides generic blanket advice rather than specific information relevant to mosquitoes. Gene flow.It would be expected that a full characterization of the technology used to make the LMO would be provided. Confined

and contained field trials could be used to evaluate the risk of gene flow and persistence. This sort of information is lacking in the guidance.

Evolutionary strategies. Evidence that LMOs exert an evolutionary effect requires considerable time and logistical considerations. The relevance of this concept in conjunction with the cost-benefit analysis of improvements to human health need to be clearly enunciated in the guidance.

Q33. Does this section include all the necessary relevant concepts?

☐ Yes

☒ No. Please comment: The section on LM mosquitoes falls short on a number of points. First, there is a well defined tiered testing approach to the release of modified mosquitoes that this sort of risk assessment would follow.

The benefits of a holistic approach using laboratory and field tests together with mathematical modelling are neglected (see Benedict et al. 2008 for the development of an appropriate overview of the RA to LM mosquitoes).

Specifically, the risk assessment misses important ecological processes such as the role of density dependence, the role of seasonality, appropriate cost-benefit analyses (i.e. the procedures needed to undertake event a small scale – involving, for example, the numbers/release sites etc). The guidance fails also to consider failures in mass rearing and the management of unintended releases. Any field release would be undertaken in a phased approach – why doesn't the guidance give any credence to this approach? Post surveillance is an essential part of any open release and the guidance provides little indication of the necessity of this sort of risk assessment/management approach.

The necessity for cultural and ethical approval for such releases can not be underestimated. The current guidance provides no appreciation that these sorts of factors are considered important in risk assessments. For contemporary approaches for this sort of risk assessment for mosquitoes see the MosqGuide initiative (http://www.mosqguide.org.uk/) and recent developments on the full risk assessment for the control of Aedes aegypti for dengue control (albeit in a non GM approach to mosquito control) (see Murray et al. 2010).

References

Benedict, M. et al. (2008) Guidance for contained field trials of GM mosquitoes with a gene drive system. Vector-Borne and Zoonotic Diseases, 8:127-166.

Murphy, B, Jansen, C, Murray, J & De Barro, P (2010) Risk analysis on the Australian release of Aedes aegypti (L.)

	(Diptera: Culicidae) containing Wolbachia. CSIRO

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: <Type here>

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. <Please type your comments here>