SUBMISSION FROM THE GLOBAL INDUSTRY COALITION (ORGANIZATION)

15 March 2011

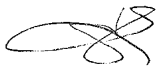
Executive Secretary
Convention on Biological Diversity
413, Saint Jacques Street, suite 800
Montreal QC H2Y 1N9
Canada

Re: Scientific review of the "Guidance on Risk Assessment of Living Modified Organisms"

Dear Sir:

Please find attached the scientific review of the “Guidance on Risk Assessment of Living Modified Organisms” submitted on behalf of the Global Industry Coalition requested in notification 2011-02-04. Thank you for the opportunity to provide our comments.

Regards,



Sarah Lukie
Executive Director
Global Industry Coalition

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: **Global Industry Coalition**

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.

We welcome the opportunity to comment on the current version of the Guidance document. As the review format is not suited for a thorough scientific evaluation, we limit our input to illustrations of where potential improvements can be made and look forward to future opportunities to develop a useful and pragmatic tool for risk assessors.

In this part of the evaluation, we ranked the usefulness of the draft guidance neutral to poor, as the current document provided no additional insights into risk assessment according to Annex III. In fact, we are concerned that this new guidance goes beyond Annex III. It proposes guidance and ideas that are not in Annex III, which will need to be pointed out below. So, this new guidance will not necessarily conflict with Annex III, but will propose things that will complicate developing regulatory systems: (1) it proposes systematic uncertainty analysis, which is a subject that is currently only academic (regulators acknowledge that any decision has some residual uncertainty, but systematic treatment of uncertainty as referenced in the

Roadmap is untested and unvalidated); (2) it limits a risk assessor's ability to use information from all LMO's in the risk assessment; (3) it proposes a standard for "scientifically sound", which does not exist (also, the AHTEG is not a standard setting body); and (4) it states that risk assessors should consider many topics that are outside the scope of environmental risk assessment e.g., food safety, ethics, liability.

The GIC believes that the Roadmap strays far from other international reference documents and publications. Assuming that such guidance is targeted to less experienced risk assessors, the Roadmap should not only refer to harmonized risk assessment approaches but should also illustrate how they have be used in risk assessment.

We again point the AHTEG to Hill, (2005) Environ. Biosafety Res. 4:67-70, which provides an excellent overview of environmental risk assessment in the context of the Annex III and is an excellent guide for improving the Roadmap.

The GIC also highlights that the Roadmap in its current form creates unnecessary ambiguity with frequent use phrases like "could cause" and "could affect". In practice, the risk assessor attains much greater certainty on what harms pose reasonable risks and what effects (hazard) testing must be done through proper problem formulation. The Roadmap fails to recognize the importance of this initial planning and testing, and leaves the reader believing that risk assessment is a never ending process of asking questions and conducting tests.

This version of the Roadmap attempts to achieve several goals: presenting an overview of the process of environmental risk assessment for LMOs, serving as a guidance document supplementing Annex III of the Protocol as well as providing links to references for risk assessors. However, it is not clear how these different objectives are achieved by the different parts of the document. For example, while the references may provide background information to a specific section, they may not be useful as such in the risk assessment process.

To assist risk assessors, the document should include a glossary for important concepts referred to in the text, especially for terms that are not defined in the Protocol. Key concepts like "protection goals", "assessment end-points", "risk thresholds" and "management strategies" have not been defined in the Protocol and have not been included in Annex III. They are not explained in the Roadmap, nor are there examples, and in consequence reference to

these undefined terms will likely confuse inexperienced risk assessors on their use. Clear definitions and didactic examples would greatly enhance the usefulness of the document.

The Protocol provides a clear distinction between movements of LMOs intended for contained use, for the intentional introduction into the environment and for the direct use as food or feed, or for processing. However, the Protocol is unclear on the matter of field trials. As such, the Roadmap is inappropriate for handling field trial requests because these cases emphasize risk management (confinement).

In addition, intentional introduction into the environment can cover research, development as well as commercial release. Although the risk assessment provided in Annex III is relevant for commercial release, the document should clarify in its scope how the guidance includes the specifics for how a risk assessor can adapt the risk assessment process to the gradually accumulated information. While the case-by-case approach is embedded, the step-by-step aspect is poorly illustrated.

There is concern that the document might be seen as biased in assuming that LMOs will have potential adverse effects. For most of the LMOs that today are subject of international movement, the risk assessments have given rise to hypothetical, potential risks rather than established adverse effects. This is not properly reflected and leaves the impression that a risk assessment would be incomplete if no potential adverse effect has been identified.

Regarding the specific points in this section of the review:

Consistency: The overall approach is consistent with Annex III, but fails to adequately elaborate on new elements. Furthermore, some indications e.g. “Related issues” go beyond the scope of the Protocol.

Scientifically sound and case-by-case manner: While some indications are provided on quality and relevance of data, it is not clear whether the use of the Roadmap will lead to a scientifically sound risk assessment. In most of the sections the only indication that is provided is a short list of points to consider, without any clarity on how these can be used in the assessment. In consequence, the risk assessment process, based on solid scientific data, can still be conducted in a scientifically unsound manner.

Various receiving environments: Several references to evaluating the impact as a function of the receiving environment should remind risk

assessors to take specific protection goals into account. Nevertheless, the reality for the LMOs deployed on large scale today is that the likely receiving environments are limited to agricultural settings and that the potential impact doesn't vary significantly between countries.

Different taxa: It is argued that the approach is applicable to different LMOs, realizing that most of the information is based on experience with plants. In principle, the approach to risk assessment should indeed be independent on the type of LMO. Yet, by limiting the points of consideration and few examples to plants, it seems difficult to support the claim that the guidance can be and will be used for other LMOs.

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: Some statements can be improved by providing indications on the consequence for the risk assessor. (*e.g.* p.2 "An LMO and its use may have several effects, which may be intended or unintended, taking into account that some unintended effects may be predictable." What is the consequence of this? How will it help to identify potential adverse effects? Similarly: "The choice of protection goals by the Party could be informed by Articles 7(a), 7(b) and 8(g) and Annex 1 of the Convention on Biological Diversity." What does "informed" mean? What is the role of the risk assessor?) Some statements are confusing (*e.g.* p.3 "The steps describe an integrated process whereby the results of one step may be relevant to other steps." As risk assessment is a structured process, it should be clarified in which cases the steps would not be relevant). Some statements may be too restrictive and divert from the case-by-case approach. *E.g.* when describing the comparative manner for risk assessment, it is argued that comparison is made with the (near-) isogenic or closely related non-modified recipient. While in early years, when there was little experience with widespread introduction of LMOs, this has been the case, it is likely that in future LMOs with a history of safe use will be used as comparators. As such, this guidance is in conflict with some of the General Principles and Points to Consider in Annex III.
Q7. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: It is indicated that the "overarching issues" can be taken into consideration again at the end of the risk assessment process to determine whether the objectives and criteria that were set out at the beginning of the risk assessment have been met. Given the overarching issues (relevancy, scientifically robustness, uncertainty) it is not clear why (and how) this should happen at the end of the process. In fact at each step, risk assessors take into account these aspects and that is why they are considered "overarching". It seems inappropriate to link them to meeting objectives and criteria at the end of the risk assessment. Setting criteria for relevancy in the context of a risk assessment is a complex issue. As will be pointed out in the relevant section, some of the information required in Annex I of the Protocol and in the guidance may not be relevant for risk assessment. While Annex III indicates different options in case of uncertainty, the guidance introduces a systematic evaluation of uncertainty and suggests that this is a standard practice. To date, there is no

internationally agreed definition of 'scientific uncertainty', nor are there internationally agreed general rules or guidelines to determine its occurrence. The discussion of uncertainty is therefore inappropriate. Uncertainty analysis is not a must in risk assessment. This section is now proposing a new requirement that currently does not exist, nor is it necessary based on the risk assessments completed to date.

The guidance recognizes that uncertainty cannot always be reduced by providing additional information. As an example, it is indicated that new uncertainties may arise as a result of the provision of additional information. However, in many cases more information will not contribute to a better understanding of the potential effect. It must be a concern for risk assessors that they only require information that will contribute to better evaluations.

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: Key concepts like "protection goals", "assessment end-points", "risk thresholds" and "management strategies" have not been defined in the Protocol and have not been included in Annex III. They are not explained in the Roadmap, there are no examples and in consequence they may confuse inexperienced risk assessors on how and when to apply them. The text on "Context and scoping of the risk assessment" (p.5) is confusing. It provides no clear guidance to risk assessors, Rather it is a set of unclearly related "aspects", some of which are policy driven whereas others are case specific (e.g. information on the non-modified recipient). In this respect there seems to be redundancy with Step 1 of the risk assessment (e.g. the identification of the "ecological function")

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: Ecological function misrepresents the "ecological" aspect of the vast majority of LMOs marketed to date and envisioned for the near future. The majority of LMOs available to date in the market and whose risks have been assessed are domesticated crops. Their function is to serve human needs. "Points to consider regarding the characterization of the LMO" lists several elements that may be required for identifying novel characteristics that could give rise to adverse effects. While information requirements are indicated, it remains unclear how these serve the risk assessment. *E.g*. information on the transformation method, characteristics of the vector, or insertion site are part of standard information set, but the risk assessor has no reference to judge the relevance of such information. Crucial information on how the LMO differs from other plants is lost in technical data requirements. In "points to consider regarding the receiving environment" a broad range of potential elements is provided. Again, the relevance for

	risk assessment may for most elements be questionable. It inappropriately broadens the risk assessment and ignores that the likely receiving environment for most LMOs has been and will be a managed system (agriculture) or a roadside.
Q10. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: It is indicated that "risk assessment is performed in five steps, as appropriate." Yet, there is no indication on what basis the appropriateness of the five steps is decided. We propose to state that if step 1 does not identify any novel genotypic and phenotypic characteristics associated with the living modified organism that may have adverse effects on biological diversity, subsequent steps are not required. When describing the comparative manner of risk assessment, it is argued that comparison is made with the (near-) isogenic or closely related non-modified recipient. While in early years when there was little experience with widespread introduction of LMOs this has been the case, it is likely that in future LMOs with a history of safe use will be used as comparators. It is remarkable that in "points to consider regarding the potential adverse effects resulting from the interaction between the LMO and the receiving environment", no reference is made to the protection goals or assessment end-points that were introduced earlier.
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 wording in "points to consider regarding the potential adverse effects resulting from the interaction between the LMO and the receiving environment" is confusing as this list includes elements of potential to cause an effect (Step 1), mechanisms via which an effect can occur (probably more appropriate in step 2) and consequences (cfr. step 3) and presents these as considerations of potential adverse effects. Specific comments: g) it should be clarified that changes in survival and/or dissemination do not automatically constitute an adverse effect *per se*. h) the potential impact would be covered under g), the additional information seems to be more related to the likely receiving environment and therefore this point is redundant. i) outcrossing and flow of transgenes are mechanisms of introgression through which certain impacts can occur, inherently they are biological phenomena. The point refers to consequences of such introgression which seems to be related to step 3. j) effects on non target organisms is only relevant in specific cases *e.g.* when the trait is directed against certain target organisms. k) cumulative effects – in this step it may be identified if an LMO has characteristics that could lead to new potential adverse effects when combined with another LMO. Whether and how this might occur –if any effect has been identified- should be addressed in step 2. (l) the point to consider is the potential for toxic or allergenic effects, the incidental exposure of humans is a mechanism for

	realizing this potential adverse effect and should be addressed in step 2 if such potential has been indicated. m) this point again combines consequence (step 3) with a mechanism, *i.e.* horizontal gene transfer (step 2). It is not clear what the potential adverse effect could be. Point n) on uncertainty seems to be incorrectly placed in the list of considerations. As we have previously emphasized, understanding the type and level of uncertainty is an inherent element in each consideration and should not be pictured as a separate effort.
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: Paragraph 2 & 3 of the rationale are confusing. Paragraph 3 suggests that other aspects are to be considered. However the two aspects that are cited are already covered in paragraph 2. Point i) - the potential to spread and establish- is a plausible pathway and therefore already covered in paragraph 2. Similarly, ii) the occurrence of adverse (e.g. toxic) effects is an identified adverse effect and therefore also covered in paragraph 2.
Q13. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: It would be better to refer to conceptual models describing relationships between the valued entity, the stressor (the LMO), and pathways of exposure and potential effects in the environment. The conceptual model for an environmental risk assessment would include the available information on the nature of the stressor, its proposed use, reasonable environmental pathways whereby exposure could occur, and potential responses of the assessment endpoint as a result of exposure. Conceptual models or scenarios that link potential effects of the activity to adverse effects on the assessment endpoints are constructed, and from these models, risk hypotheses for testing are derived. The risk assessor, in conjunction with decision-makers, must judge whether particular scenarios are sufficiently plausible to warrant further evaluation, because it is possible to produce an infinite number of logical pathways that lead to harm, but most can be ruled out as so unlikely that their further assessment is unnecessary. Relevant publications: - Nickson, T. (2008) Planning Environmental Risk Assessment for Genetically Modified Crops: Problem Formulation for Stress-tolerant Crops. Plant Physiol. 147: 494-502. - Patton, D.E. (1998) Environmental risk assessment: tasks and obligations. Hum Ecol Risk Assess 4:657–670 - Raybould, A. (2006) Problem Formulation and Hypothesis Testing for Environmental Risk Assessments of Genetically Modified Crops. Environ. Biosafety Res. 5: 119-125. - Wolt, J.D., Keese, P. Raybould, A., Fitzpatrick, J.W., Burachik, M., Gray, A., Olin, S.S., Schiemann, J., Sears, M., Wu, F. (2010) Problem formulation in the environmental risk assessment for genetically modified plants. Transgenic Research 19: 425–436.

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: When comparing the "points to consider" there is a striking similarity with points mentioned in step 1. It may therefore not be clear to a risk assessor what exactly should be done in this step and how the information should be considered. Point f) on uncertainty seems to be incorrectly placed in the list of considerations. We argued before that understanding the type and level of uncertainty is an inherent element in each consideration and should not be pictured as a separate effort.

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: This section should be edited to avoid confusion. For example, on p.10 reference is made to "the consequences of (i) agricultural practices, such as the level of inter- and intra-species gene flow, dissemination of the recipient" considered as consequences of agricultural practices. It is unclear how "gene flow" and "dissemination", two biological features, can be considered a consequence of agricultural practice. Some of the points to consider seem to be out of place and should rather be part of step 1 and/or step 2. Point b) identifies "Adverse effects which may be direct and indirect, immediate and delayed". This is relevant in step 1 or step 2 when defining certain adverse effect and mechanisms. It is not clear how this can be used in evaluating consequences. Point c) refers to results from laboratory experiments and field trials that seem more appropriate when discussing the potential adverse effects (step 1). It could be argued that in step 3, a combination should be made between the potential adverse effect (step 1) and exposure/mechanism (step 2), but in fact this is what is performed in the evaluation (step 4). Also point d) referring to possible adverse effects that may occur, after introgression, due to the expression of the transgenes in the sexually compatible species; seems to be in an incorrect position and should rather be included in step 1.
Q16. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: See comments on Q15
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: Given the comments made above, this section provides little insight in what the risk assessor is expected to do. Point e) on uncertainty seems to be incorrectly placed in the list of considerations. As we have previously emphasized, understanding the type and level of uncertainty is an inherent element in each consideration and should not be pictured as a separate effort.

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: Points (d), (e) and (f) in the Points to Consider in Step 4 should be deleted. They are presented in a manner that is vague and may not apply in all cases. Point d) addresses interactions between identified individual risks. This has not been explained before and either would fit in step 1 or in step 2. Similarly it has been argued that potential cumulative effects (point e) should be addressed in step 1 and/or in step 2. In this way, both aspects will be included when all previous steps are incorporated in the overall evaluation in step 4. Point f) on uncertainty seems to be incorrectly placed in the list of considerations. As we have previously emphasized, understanding the type and level of uncertainty is an inherent element in each consideration and should not be pictured as a separate effort.
Q19. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: In the rationale it is mentioned that in step 4 it should be determined whether the assessed risks meet the criteria set out in the protection goals, assessment endpoints and thresholds, as established in relevant legislation of the Party or in its practice. This is the first time since discussing the background of risk assessment that protection goals, assessment endpoints and thresholds are introduced. Again this is done without a clear reference to how this can be done in practice. It could be argued that step 4 is merely the estimation of the overall risk, whereas any evaluation of acceptability should be left to step 5. As it is presented now, there is no clear distinction between step 4 and step 5.) It is also noted that there is no universally accepted method to estimate the overall risk but rather a number of methods are available for this purpose. And that "the outcome of this step may be, for example, a description explaining how the estimation of the overall risk was performed." It is unrealistic to suggest limiting the outcome of this step to a description of the methodology and this should be clarified.
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: See Q18 & Q19 indicating that an inexperienced risk assessor may easily be confused by the different indications.

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:

	Step 5 is introduced as “an interface between the process of risk assessment and the process of determining whether risk management measures are necessary”. It is not common that the assessment and the determination of management measures are presented as separate processes, in particular as they are tightly linked as stated in step 5 and Annex III. It could be interpreted that management measures may depend on other considerations not based on the risk assessment. The text is biased towards identified risks. It seems to neglect that in the actual cases completed to date no increased risk has been identified. All monitoring conducted to date is the result of prescriptive regulatory requirements or product stewardship and is not directed by potential adverse effects (*e.g.* as it cannot be excluded that target pests develop resistance to a certain crop protection strategy, insect resistance management schemes have been established as a good practice for enhancing sustainable use).
Q22. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: When management measures are selected, they may address identified risk as well as uncertainties. They should be proportionate to the level of risk and to the level of uncertainty respectively. A distinction should be introduced between management measures and monitoring and their respective deployment justified by the risk assessment. They should not be considered as prescriptive elements of every risk assessment outcome. It is indicated that the “overarching issues” can be taken into consideration again at the end of the risk assessment process to evaluate whether the objectives and criteria that were set out at the beginning of the risk assessment have been met. Noting that the overarching issues are taken up in every step of the risk assessment and that the objectives are defined by protection goals, assessment end-points and risk thresholds, it is not clear what this additional consideration will contribute and how it should be performed. It is not clear how point (c) “the feasibility of the adoption of risk management or monitoring strategies” is a point to consider when evaluating the acceptability of risks. This gives an outlook on the chances that a selected management strategy will be performed, and is not related to the risk assessment or to the efficacy of the measure.
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: Discussing identified risks, the focus is on risks that are not acceptable in relation to the established protection goals, assessment end-points and risk thresholds. In order to apply this, risk assessors would require more information on these essential concepts.
3. RELATED ISSUES	
Q24. Does the “Related Issues” section include all relevant issues related to risk assessment and decision-making process but	☐ Yes ☒ No. Please comment:

that are outside the scope of the Roadmap?	In the introduction of the Roadmap it is indicated that other articles of the Protocol or other relevant issues may also be taken into account in the decision-making process. However, the section on "Related Issues" is irrelevant, misguiding and confuses elements already included in risk assessment with broader policy and technical issues. The fact that they are indicated as outside of the scope of the Roadmap, even extending beyond the scope of the Protocol, justifies removing this section completely. Risk management related to the introduction has been addressed in step 5. The only additional provisions for decision making provided by the Protocol relate to the possibility for public consultation and for socio-economic considerations arising from the impact of living modified organisms on the conservation and sustainable use of biological diversity, especially with regard to the value of biological diversity to indigenous and local communities. Capacity-building, liability and redress are dealt with independently and should not influence decision-making. To some extent, they rely on the fact that a functional risk assessment and decision-making process is in place. Finally, consideration of ethical issues is not in the scope of the Protocol. Also co-existence is not defined in the Protocol and even in countries that implement such policies, it is explicitly separated from the environmental 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: <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: This guidance is misleading to the uninitiated risk assessor since it fails to point out that some Parties and non-Parties do not regulate stacked trait products. The following condition should be included "in cases where the stacked trait product must undergo a risk assessment". While implicitly indicated in the text (*e.g.* using the word "re-examination" suggests that information has been examined already), this additional guidance assumes that single events have been evaluated. The reality today is that a broader diversity of options is presented, sometimes only offering a higher level stack of events. The guidance should therefore clarify the assumptions on which it is based. If the considerations are relevant, it is not clear what they add to the steps that were already described in the Roadmap document. They do not provide useful guidance for the risk assessor. *E.g.* on p.15 it is indicated that "the reappraisal of the molecular sequence at the insertion sites, and the intactness of the transgenes may be

	confirmative to the molecular characteristics of the parental LMOs, but may also be a basis for assessing any intended or unintended possibly adverse effects on the conservation and sustainable use of biological diversity in the likely potential receiving environment and of potential adverse effects on human health." How this information can effectively be used for assessing possibly adverse effects is not further indicated. This section also refers to "unintentional stacked events". These are already fully covered in step 1 of the Roadmap. Finally a specific topic is suggested on the development of detection tools for distinguishing the combined transgenes in a stacked event. All methods routinely used today allow detection and identification of single transformation events. It is correctly stated that methods used to detect single events will not differentiate between a mixture of single transformation events and the same events being part of a stacked event. Nevertheless, these methods can be used and allow a very detailed identification of the material whenever required, pointing out that "a special problem may arise particularly in the cases where the stacked event contains multiple transgenes with similar DNA sequences. Therefore, the detection of each and all individual transgenes in a stacked event may become a challenge and needs special consideration" is misleading.
Q27. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: In the Roadmap guidance is provided on the steps and considerations that are used when conducting a risk assessment for an LMO. This Annex has the objective to give additional guidance on the risk assessment of LMOs with stacked events generated through conventional crossing of single or multiple event LMOs (for the time being restricted to plant LMOs). The only justification for a specific Annex seems to be the fact that a growing number of LMOs with stacked transgenic traits are developed. Yet, there is no justification on the basis of specific potential adverse effects that could result from the stacking. Again, the Annex neglects the fact that different countries treat stacked events in different ways. Some have chosen to regulate stacks as new LMOs, requiring an additional risk assessment for such combination. Others have chosen to include future stacks in the initial approval of the single (or lower level stack LMO), only requiring additional information if new data would illustrate that a specific combination could lead to new potential adverse effects. Both approaches are compatible with the Protocol, and it is striking that this Annex seems to suggest that any new stack would require a risk assessment.
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 on Q26 & Q27
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: In the Roadmap guidance is provided on the steps and

	considerations that are used when conducting a risk assessment for an LMO. This Annex has the objective to give additional guidance on the risk assessment of living modified (LM) crops with improved tolerance to abiotic stress. However, there is no body of experience to date on LMOs with abiotic stress traits from which to create guidance. Aside from a limited number of appropriate publications, this area is still under development. At best, this guidance should only reiterate the principles in the improved Roadmap. In fact this is also illustrated by the questions that are highlighted under risk assessment as potentially relevant. None of these are specific for LM crops with tolerance to abiotic stress and are already addressed in the approach presented in the Roadmap. Again, none of the considerations (characterization of the LM crop with tolerance to abiotic stress in comparison with its non-modified crop, unintended characteristics and increased persistency in agricultural areas and invasiveness of natural habitats) are specific for LM crops with tolerance to abiotic stress. The main concern seems to be the comparative approach that should take into account proper testing conditions and proper controls, a requirement that is encompassed in the “overarching issue“ of a sound scientific approach. The authors recognize that the (adverse) effects may exist regardless of whether the tolerant crop is a product of modern biotechnology or conventional breeding, yet indicate that specific issues may be more relevant in the case of abiotic stress tolerant LM crops. They fail to indicate why this is the case and how this will affect the risk assessment. They also fail to indicate how this would affect step 5 of the risk assessment where the potential effect of the LMO needs to be evaluated in relation to other effects. It is speculated that in the future, information available from “omics” technologies, for example, “transcriptomics” and “metabolomics”, may help to detect phenotypes that cannot be detected using a comparison between field grown plants at a suboptimal condition. This speculative statement in an Annex to the guidance should be deleted as it is does not reflect the technical state-of-the-art in risk assessment. It must be pointed out that such methods have not been validated, that it is not the common practice today to rely on such information for risk assessment and that further research will be required before any conclusion can be supported by such techniques. For a recent review see Ricroch A.E., Bergé J.B. and Kuntz M. (2011) Evaluation of genetically engineered crops using transcriptomic, proteomic and metabolomic profiling techniques Plant Physiology Preview. Published on February 24, 2011, as DOI:10.1104/pp.111.173609
Q30. Does this section include all the necessary relevant concepts?	☐ Yes ☒ No. Please comment: The concepts that are included are not specific for LM crops with tolerance to abiotic stress.
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 comments Q29

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: <Type here>
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. LMO risk assessment has been fine-tuned over more than 20 years. The Roadmap presents an opportunity to integrate this experience and to provide a workable tool for less experienced risk assessors. This requires very clear guidance, educational examples and precedents and links to relevant information sources such as the ICGEB and CERA database. Special care should be taken to avoid confusion in terminology and recommendations. On the contrary, the effort should lead to harmonization of the approach.

Against the background of the legitimate objectives of the Protocol, the main objective deploying LMOs is further improvement in vital sectors like agriculture, food, medicine and industrial products. The identification of potential risks and uncertainties needs to be weighed against the risk of failing to adopt new solutions in a timely manner.

Lastly, as previously stated, the specific documents in Part 2 are also problematic. The document that addresses "risk assessment of LMOs with stacked genes or traits" is misleading as it does not point out that some Parties and non-Parties do not regulate stacked trait products. The document that addresses "risk assessment of LM Crops with tolerance with abiotic stress" does not reflect the fact that there is simply no body of experience to draw on for LMOs with abiotic stress traits for the purpose of developing useful or relevant guidance.