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OPEN-ENDED ONLINE FORUM ON RISK ASSESSMENT AND RISK MANAGEMENT

Note by the Executive Secretary

1. In decision CP-VIII/12, the Conference of the Parties serving as the meeting of the Parties to the Cartagena Protocol on Biosafety extended the Online Forum on Risk Assessment and Risk Management to exchange experiences on risk assessment, provide information and views on, and perceived gaps in existing guidance materials, and proposals to address any gaps identified. Furthermore, the meeting of the Parties invited its Bureau to appoint a lead moderator to moderate and report on the online discussions.

2. Discussions under the Open-ended Online Forum on Risk Assessment and Risk Management were convened through the Biosafety-Clearing House from 29 January to 12 February 2018, and moderated by Mr. Timothy Strabala of New Zealand[1]. The topics of discussion were drawn from the decision, as follows:

(a) Sharing experiences on risk assessment of living modified organisms;

(b) Information and views on existing guidance materials on risk assessment;

(c) Perceived gaps in existing guidance materials on risk assessment, and proposals to address any gaps identified.

3. The annex to the present document presents the final report of the online forum, as prepared by the lead moderator.

Annex

REPORT ON THE ONLINE FORUM ON RISK ASSESSMENT AND RISK MANAGEMENT

Prepared by Mr. Tim Strabala, moderator

1. In its decision CP-VIII/12, the Parties to the Cartagena Protocol decided to extend the Online Forum on Risk Assessment and Risk Management to exchange experiences on risk assessment, provide information and views on, and perceived gaps in existing guidance materials, and proposals to address any gaps identified. Based on this, the Open-ended Online Forum on Risk Assessment and Risk Management was convened through the Biosafety-Clearing House between 29 January and 12 February 2018. A total of 110 interventions were made during that period, by 48 different participants, among which 31 were nominated by Parties, 2 by non-Parties and 15 by organizations. There were in total 64

* CBD/SBSTTA/22/1.

[1] The discussions are available at: https://bch.cbd.int/onlineconferences/forum_ra/discussion.shtml

interventions made by parties, 5 from non-parties, and 41 from organizations. Breaking these numbers down by the three topics of the forum, there were 27 interventions in Topic 1 from 25 participants, 28 interventions in Topic 2 from 27 participants, and 54 interventions from 40 participants in Topic 3. There were 17 participants that submitted at least one intervention in each of the three Topics.

2. The topics of discussion were drawn from decision CP-VIII/12 as follows:

(a) Sharing experiences on risk assessment of living modified organisms;

(b) Information and views on existing guidance materials on risk assessment;

(c) Perceived gaps in existing guidance materials on risk assessment, and proposals to address any gaps identified.

3. The present document provides an overview of the views shared through the online forum. For a full account of all views, it is recommended to refer to the original online interventions through the Biosafety-Clearing House (https://bch.cbd.int/onlineconferences/forum_ra/discussion.shtml). Although the overwhelming majority of interventions stayed on topic, there were a few submissions that did not fit with any of the topics with which participants were tasked, and so were not included in this summary. It is also noted that, due to the interrelated nature of the three topic areas, there were some references in comments in one topic that also had relevance to another topic, most notably where comments in Topics 1 and 2 had relevance to more extensive discussion in Topic 3. These linkages are now noted where they occur, with suggestions that the reader examines Topic 3 for additional detail.

4. In addition to the summaries of the three topic areas, a bibliography of links and references provided by various forum participants as additional sources of information for risk assessors who seek additional guidance and/or background information on risk assessments has been compiled. This is consistent with discussions at COP-MOP 8, that the online forum could serve as an information resource for Parties and risk assessors seeking additional information and guidance.

Topic 1: Sharing experiences on Risk Assessment of Living Modified Organisms

Experience on information sources for risk assessment

Biosafety Clearing House/3rd national reports

5. Some submitters noted that there is considerable experience in risk assessments for many different types of living modified organisms (LMOs), and suggested that risk assessors look to the BCH as a platform for information regarding risk assessments for these organisms. Another intervention suggested that the support from the roster of experts could be useful for RA.

6. Regular survey of BCH entries for new decisions and risk assessments is useful to gain insights on what factors others have considered in issuing approvals of specific LMOs, or their rationale for declining their use. The BCH is a useful gateway to the websites of scientific societies and international organizations to review and update information and anticipate new LMOs that may require risk assessments and regulatory approvals.

7. One participant suggested the 3rd national reports as a source of information on parties' experiences in conducting risk assessment, noting that many countries have reported having conducted at least one risk assessment and some of these have also indicated they have done so using the AHTEG guidance[2].

8. This intervention led to some discussion on the point of potential inadequacies and/or gaps in both governmental guidelines and the AHTEG guidance on risk assessment. Another intervention noted that although some countries might have submitted information that they do not apply the AHTEG

[2] Refers to 'Guidance on Risk Assessment of Living Modified Organisms and Monitoring in the Context of Risk Assessment' that was developed by the RARM AHTEG, and noted by the Parties in the decision CP-VIII/12 in 2016. The document is referred to in this summary as 'the AHTEG guidance'.

guidance itself, this does not exclude the possibility that they might use it as a background document to develop their own official guidance.

Governmental guidance documents and approaches to risk assessment (RA)

9. Many submitters suggested looking at the RA guidance documents used by other governments, many of which are happy to share their information that may be helpful for risk assessment, as well as again suggesting the BCH as a resource to access them. One submitter suggested comparing guidance documents to find similarities and differences. Documents such as the OECD consensus documents on crop plants and traits, as well as those of the IPPC[3], the OIE, OGTR, ILSI, ICGEB, WHO and FAO were discussed as good sources of information which are revised periodically and provide insights that help evaluate options in the context of needs and protection goals.

10. A submitter from India noted the legislative measures to implement biosafety in that country. These Environment (Protection) Rules led to the enactment of Rules for GMOs, which require the review of scientific advancements and the issue of manuals/guidelines for risk assessment and risk management.

11. A participant from the Philippines discussed risk assessments of LMOs for contained, confined, and large scale cultivation of LMOs, noting that there has never been an incident where the introduction of LMOs has harmed their biodiversity, and concluded by noting that their existing guidance documents in addition to risk assessments done by other countries are sufficiently robust to allow a country to reach a decision on whether or not to adopt this technology.

12. A participant from New Zealand noted that their legislation dictates their approach to risk assessment. This approach requires the assessment of potential benefits, and the imposition of risk-mitigating controls (if necessary) that usefully affect the risk/benefit balance. The same participant also highlighted key principles of risk assessment: process transparency, a case-by-case approach, definition of scope, description of the process, identification and description of uncertainties, dialogue between risk assessors and managers, risk/benefit/mitigation analysis, and peer review of risk assessments.

13. A participant from Brazil noted the approval of 117 LMO events in different organisms (crops, tree, mosquito, microorganism, vaccine) by its National Biosafety Technical Commission. The participant further noted that risk assessments in Brazil are conducted using three general principles: 1) case-by-case; 2) evidence-based; 3) the use of an iterative process. The methodology used for RA is based on Annex III of the CPB and Codex Alimentarius. Any new organism with a new trait is evaluated using a risk hypothesis created by experts to ensure the assessment is as robust as current knowledge allows.

14. A participant noted that the Office of the Gene Technology Regulator (OGTR) in Australia has broad experience in GMO risk assessments and that monitoring trials is used to improve later risk assessments and management plans, which they make available on the OGTR website (see Appendix). Commercial scale releases are listed on both the BCH and OECD Biotrack databases. The participant further noted that OGTR also publishes supporting information on GMO parent organisms and references on methods of genetic modification and selectable markers, and that OGTR shares its experiences with visiting delegations and at workshops internationally.

15. A participant stated that Thailand had developed guidance consistent with the AHTEG guidance document, noting that the requirements of a risk assessment vary depending on the characteristics of the LM plant being assessed. Another point made by this participant in relation to experiences in conducting risk assessment is the challenge in distinguishing what information is “need to know” versus “nice to know”. It was pointed out that, in some cases, this is a reason for failure in finding consensus among risk assessments.

16. A participant from the Czech Republic noted that the Committee for GMOs and Products has 20 years’ experience in monitoring field experiments of GM crops and trees (e.g. maize, winter oil seed rape, potato, flax, sugar beet, plum), for various potential environmental impacts. Results and practical findings of this work have been obtained and used for RA.

[3]Please see the List of Acronyms (Appendix 2)

17. A participant from Japan noted the environmental release approvals for agricultural purposes of more than 130 LM events after environmental risk assessment. Species released include alfalfa, carnation, oilseed rape, soybean, sugar beet, corn, papaya, rose, cotton, silkworm, and a live vaccine for animals. The participant further noted that approvals and assessment reports are available in the national Biosafety Clearing House of Japan (see Appendix for link) as well as in the central portal of the BCH.

18. A participant from the United States of America pointed out the need for RARM to include expertise that recognizes our current understanding of the innate plasticity of genomes (eg, transposable elements, etc.), and that genetic changes in and of themselves are not indications of likely environmental risks. The submitter also noted that countries have worked in a variety of international forums to develop practical, systematic approaches to evaluate the environmental safety of all organisms, regardless of the genetic modification techniques that might have been used (eg, plant pathogens and arthropod pests, as well as those problematic or undesirable plants that are often referred to as "weeds"). Finally, the submitter noted the mutual benefits gained from the technical exchanges among environmental risk assessors, including the decades-long technical discussions held among assessors of the United States, Canada, and Mexico. A key finding of these exchanges is that government regulatory agencies use similar approaches for risk assessments, even if the terminology or legal frameworks used may be different.

19. This intergovernmental cooperation was echoed with an intervention stating that cooperation between organizations can strengthen the implementation of risk assessment. An example given was the information exchange between the Commission on Phytosanitary Measures (CPM) and the IPPC Secretariat.

Other guidance for RA

20. One submitter noted that risk assessments can be conducted adequately using the methodology in Annex III of the CPB. Another noted that there is experience in risk assessments for the accidental and controlled release of genetically modified mosquitoes that conforms to the standards recommended by the US National Academies of Sciences, Engineering and Medicine for gene drive modified organisms and synthetic biology. This provides insights into some of the challenges of such assessments. A third participant noted that the use of a risk assessment matrix could help keep the RA process focused. Moreover, an important step will be to distribute documents in languages other than English.

21. Another intervention noted the long history of discussions on the topic of development of additional guidance. This participant noted that in the discussions over the years between 2005 and 2016 there was an "…overwhelming consensus by the Parties that the existing guidance should apply to all types of LMOs." In a similar vein regarding the AHTEG guidance, the participant noted that in discussions since 2009, some participants have concluded that the guidance is adequate, and that others have disagreed.

Shortcomings in information limit risk assessment

22. A few interventions discussed perceived data shortfalls that may prevent a complete risk assessment from being achieved. Specifically, shortcomings in data including molecular analytical data, as well as a lack of data regarding indirect, long-term and complex environmental interactions with target and non-target organisms and the abiotic environment, were noted.

Other experiences pertaining to RARM

23. A few interventions discussed experiences pertaining to overall approaches to risk assessment and risk management. One participant advocated the use of probability theory, and the adoption of a Bayesian approach to risk calculations, while noting that successful implementation requires careful coordination of experimental/observational studies with these activities.

24. Another intervention noted the need for attention to centres of genetic diversity in considering risk assessment and recommended the book "Ethnobotany of Mexico: Interactions of people and Plants in Mesoamerica", specifically Chapter 21 titled: "Biosafety and Environmental releases of GM crops in mesoamerica: Context does matter" (see Appendix).

25. Other challenges noted were in ensuring that risk assessors take a multi-disciplinary approach to their work, as well as effectively communicating the points and conclusions of the risk assessment to decision makers in non-technical terminology.

Comments on practical experience and training

26. A theme expressed in some posts reflected the view that information pertaining to the risk assessment process or methodologies is sometimes not well understood due to a lack of practical experience. Additionally, the view was expressed that sufficient guidance (or lack thereof) is not the main challenge for many risk assessors. Rather, administrative and organizational issues result in individual or institutional challenges in carrying out risk assessments. See Topic 3 for additional discussion on this point.

27. A recommendation was put forward that efforts should be made toward improving knowledge and understanding regarding the objectives, use, general principles, and methodology of risk assessment. The International Centre for Genetic Engineering and Biotechnology (ICGEB; see Appendix for link) was suggested as a useful source for training.

Topic 2: Information and views on existing guidance materials on risk assessment

Overview

28. Discussion in this topic was notable in that there was some agreement that, in one form or another, existing guidance on risk assessment is useful. However, there were divergent views amongst participants as to which guidance documents were perceived as useful, with some preferring the AHTEG guidance and others preferring other existing documents, and still others suggested that the AHTEG guidance is used as one tool among others in the conduct of a given risk assessment. A few submitters noted that additional guidance on specific topics of risk assessment are still needed, which is covered in detail with interventions under Topic 3.

Issues and principles to consider in RA

29. One submitter stated that issues to consider in risk assessment of LMOs should include the likelihood of gene transfer to other organisms, impacts on human and animal health, the likelihood of realizing potential adverse effects, estimation of overall risk, and possible consequences. Another submitter noted that risk assessment is an interdisciplinary process, and the key is to find the right document that is best helpful to the specific case at hand. A third submitter suggested that international standards should be put forward/developed to make risk assessments more scientific and reasonable.

AHTEG guidance

30. Many submitters noted that the AHTEG guidance is a useful tool to assist in conducting risk assessments in accordance with the Cartagena Protocol, providing an adequate general basis for RA, as well as for the species covered in Part II of the document. Some submitters noted that this guidance had undergone many years of testing, review, and revision. Another submitter noted that the guidance was primarily for risk assessment of plants, and that a risk assessor with knowledge of other organisms may be able to adapt the guidance for those species. Other submitters noted references to other guidance documents in the AHTEG guidance that pointed risk assessors to other potential sources of information, including medical GMOs and risk assessment of GMOs and GM-products if needed.

31. Several submitters noted that there are many guidance materials on risk assessment available worldwide that are in accordance with Annex III of the Cartagena Protocol in addition to the AHTEG guidance. The submissions echo those in Topic 1, stating that many of these guidance documents are readily found in the BCH.

Perceived inadequacies in AHTEG guidance

32. A few submitters noted the view that there were some inadequacies in the AHTEG guidance, which they expanded on in Topic 3. One submitter noted that "The existing guidance produced by the AHTEG is true to the literal wording of Annex III of the Protocol, but mainly limited to paragraphs 8 and 9. Risk assessors might benefit from more development of what is called for in paragraph 3 (ie, risk assessment should be carried out in a scientifically sound and transparent manner, and can take into account expert advice of, and guidelines developed by, relevant international organizations)", suggesting that the indicators of 'soundness' and 'transparency' are not clear, and calling for the development of guidance on these terms in the context of risk assessment.

33. Another submitter asked how expert advice and other guidelines, which might conflict, should be taken into account, and what the criteria for determining 'expertise' were. A third submitter suggested that additional and specific guidance on how to achieve a high quality scientific risk assessment in the context of the release and use of synthetic biology products would be beneficial to the international community. The submitter suggested that this would provide an opportunity to better align the CBD's recommendations with those of the US National Academies of Sciences Engineering and Medicine (also expanded upon in Topic 3 discussion).

34. Some submissions suggested the expansion of Part II of the guidance, both in general terms and specifically for the inclusion of information about how the risk assessment of living modified animals (other than mosquitoes) should be considered.

35. As a counterpoint to this view, one submitter stated: "There is a general misunderstanding amongst us on what constitutes risk assessment methodology, and what is meant under "gaps" in existing guidance materials."

36. One submitter suggested that the AHTEG guidance document was full of information that could help the risk assessment process, but is "…too long, confusing and difficult to follow", and thus does not contribute to the establishment of regular standards for Parties to generate their own regulatory systems.

Other guidance documents

IPPC guidance

37. One intervention suggested that the material and technical recommendations in the IPPC documents such as "LMOs, biosecurity and alien invasive species" and "Overview on International Standards for Phytosanitary Measures (ISPMs) and their application to living modified organisms (LMOs)" (See Appendix for links) could be useful to risk assessors.

EFSA guidance

38. Several submitters noted that the EU has guidance documents generated by the EFSA GMO Panel on LMOs plants, microbes, mammals, fish and mosquitoes (see Appendix for link). Another submitter noted the existence of regional documents, including various OECD documents and the EFSA guidance documents, in addition to many national Guidance Documents as potential sources of useful additional information.

Annex III of the Cartagena Protocol

39. One intervention suggested that Annex III of the Cartagena Protocol is a well-established risk assessment methodology that is valid for all cases of risk assessment. The submitter noted that the Annex III methodology is flexible and recognizes that "the process of risk assessment may on the one hand give rise to a need for further information about specific subjects, while on the other hand information on other subjects may not be relevant in some instances."

40. Another intervention noted that some Parties established guidance documents for risk assessment based on Annex III and have posted them on the Biosafety Clearing House and/or their national websites.

The post also noted the availability of guidance materials from other international organizations such as the OECD Working Group on Harmonization of Regulatory Oversight in Biotechnology.

Guidance from Parties can be found on BCH and other sources

41. One submitter noted that the Roster of Experts is an important potential source of information regarding questions on how to implement existing guidance on complicated cases of risk assessment. Another submitter noted that guidance materials, as well as examples of risk assessment and risk management applied to LMOs, are readily available through the BCH (and other websites).

42. One submitter noted many sources of information, including those listed above, but also the CODEX Principles for the Risk Analysis of Foods Derived from Modern Biotechnology together with OECD Consensus Documents (see Appendix under "Guidance Documents") as an excellent basis for any country to develop their regulations and procedures for risk assessment of LMOs. The intervention also noted various scientific papers, national guidance documents, the ISPM11 manual from IPPC; the Biosafety Resource Book from FAO, the BCH virtual library, and previous discussions on this online forum.

The need for additional guidance on specific topics

43. Many submitters suggested that existing guidance documents are more than sufficient for any currently conceivable risk assessment, and that there is no need for the development of new guidance, either generally, or for specific organisms or classifications of organisms. Several risk analysis frameworks were specifically mentioned (see Appendix for details). One submitter expanded on this point by stating that "The robustness of a regulatory process comes with real time experience and therefore use of available documents as a starting point seems more practical." National experts in this context were also mentioned in another intervention. Another submitter noted that although "…the methodology of risk assessment is founded on sound scientific principles, and is unlikely to change over time, specific considerations as part of the case-by-case risk assessment evolve over time reflecting on new scientific knowledge and technological progress that are readily addressed with the developments in the field of regulatory sciences." See Topic 3 summary for additional discussion on this point.

Inclusion of benefits assessment in the risk assessment

44. A few interventions mentioned the need for a benefits assessment to be done in tandem with risk assessments to help define an acceptable risk endpoint in the assessment. Like the perceived risk assessment gaps discussed above, this idea is expanded upon substantially in Topic 3. One intervention suggested that "The consideration of this information could help with the risk communication and to a better understanding of the decision-making process that leads to the decisions the Parties governments are making." Another intervention stated that potential benefits can be assessed in the same way as risks. See Topic 3 summary for additional discussion on this point.

Development of national RA guides consistent with CPB

45. A final point under this topic was that the end goal of all Parties conducting risk assessment of LMOs is to eventually develop their own guidance and methodology that suits their particular circumstances, experiences, and "…protection goals, final assessment endpoints, ecosystem services, centres of origin and genetic diversity, use of herbicides and so on, following the provisions of the Cartagena Protocol."

Topic 3: Perceived gaps in existing guidance materials on risk assessment, and proposals to address any gaps identified

Overview

46. Topic 3 was the most active and also involved the most direct debate (most of which occurred in the final six hours of the two-week forum). Views ranged from the lack of gaps in existing guidance

materials (and thus no need to develop more), to a wide array of topics that were put forward as needing more development, including benefits assessment. The discussion also included suggestions for the establishment of a process for establishing whether a gap exists and how to address it.

Perceived shortcomings/gaps in the AHTEG guidance

Perceived shortcomings

47. One submitter suggested that the guidance document is too long, and Part II on specific types of LMOs and traits is confusing to new users of the document. The intervention suggests removing Part II of the document, retaining only Part I and III of the document as the general road map for risk assessment, risk management and monitoring. The intervention further suggests that Part II can be set aside as case studies for specific LMOs/traits as a separate document. The submitter also suggested that actual case studies on specific organisms, particularly for the most common LMO traits, would be more appropriate, that more clarity is needed on unforeseen long term effects of LMOs, and that the risk estimation scale should somehow be standardised by experts to make it less subjective.

48. Another submitter suggested the opposite regarding the AHTEG guidance in that it is written too generically and at too high a level with little or no specific detail on how to achieve the document's aspirations (eg, conduct a "scientific risk assessment").

49. Another submitter suggested that it is necessary to introduce examples of various monitoring types including development of ecological experiments for confined and large scale field trials.

Perceived gaps in the AHTEG guidance

50. A few submissions suggested that information on risk management/mitigation was lacking. LM plants with stacked genes and LM plants with abiotic stress tolerance were mentioned specifically. The submitter suggested that the sensitivity and reliability of the mitigation strategies and monitoring techniques need to be included

51. One submitter suggested that the guidance could be improved through the inclusion of more specific topics. The submitter was interested in guidance on the type of technology that was used to create a given LMO. Other submitters were of different views arguing that a process-based approach would displace the focus of risk assessment from the characteristics of the LMO to the technology or processes used in its development. .

General comments on perceived gaps across all guidance documents

52. One intervention stated that Parties to the Cartagena Protocol on Biosafety have identified their needs and priorities for further guidance on risk assessment, including in response to Decision VIII/12. The submitter states that this is presumably because there is a perceived gap in existing guidance materials on risk assessment.

Perceived gap between NASEM recommendations and AHTEG recommendations

53. One submitter expressed concern regarding the recommendations of the quantitative/modelling approach to risk assessment of the US National Academy of Science Engineering and Medicine, as compared to the more qualitative approach of the AHTEG guidance. The submitter notes that qualitative risk assessments are easier to conduct but they are inherently unscientific because their terms eg, "highly unlikely", are not defined. The submitter asserts that risk-endpoint specific experiment and analysis standards, would help streamline the risk assessment process and provide a platform for consistency between assessments. This was echoed in another intervention with the suggestion of the addition of links to academic papers on the subject.

54. Other submitters noted that quantitative risk assessments would be extremely difficult for risk assessors in some countries to achieve, due to lack of experience and resources. Furthermore, they noted that such quantitative assessments were not always necessary, particularly in cases where the trait/species combination is well understood. The intervention urges not adding to the regulatory burdens of countries

that have many other urgent problems. Another submitter agreed with these points and referenced a 2011 paper: "A semi-quantitative approach to GMO Risk-Benefit Analysis" (see Appendix for reference). The approach is intended for risk assessors in developing countries, and does not require sophisticated software or a background in mathematics and statistics.

55. Another submitter noted that he had seen many methodological improvements to the experimental approach to collecting and analysing data, but he did not see a workable path to creating guidance on making methodological improvements, due to their generally ad hoc nature, resulting from scientific advances, rather than changes to guidance.

56. Another submitter noted that: "…a quantitative approach is not necessarily any more objective or precise than a qualitative approach, and invariably there are challenges regarding initial assumptions, describing the quantitative model, and communicating the results.

Perceived gap in consideration of benefits

57. There was extensive discussion on a perceived gap in the consideration of a risk/benefit balance in LMO assessments, with many submitters putting this issue forward as a perceived gap, particularly as it is perceived to have slowed the introduction of LMOs in many countries around the world. One submitter noted that: "In the absence of any consideration of benefit, there is no clear end point to determine how much risk (if any) is acceptable. But if the two are considered together, it is much easier to decide whether the benefits outweigh the risks." The submitter went on to suggest that perhaps the so-called "venture principle" should be taken into account in addition to the precautionary principle.

58. The Precautionary Principle was also identified by one submitter as a "flawed paradigm" of the Cartagena Protocol, in addition to the lack of benefits analysis. Another submitter considered that benefits should also be considered within the scope of the Protocol, because this is consistent with the dual purpose of the protocol, to provide 'an enabling environment for the environmentally sound application of biotechnology, making it possible to derive maximum benefit from the potential that biotechnology has to offer, while minimizing the possible risks to the environment and human health.' The submitter went on to suggest that "guidance on risk assessment under the Protocol should go beyond a strictly precautionary consideration of the risks to include some means by which to consider benefits in the decision-making process."

59. Other submitters made mitigating statements in response to these assertions. One submitter suggested that there was not a 'gap' *per se*, and regardless, "there is no realistic opportunity for a group convened at the international level to develop something more useful than what is already in existence." Another submitter did not wish to make a statement on whether a gap existed, but rather, simply say that "…the most useful guidance will take not only risk into account, but also potential benefit, as well as risk mitigation strategies." A third submitter stated: "While it will certainly not be necessary to carry out an elaborate benefit analysis for any activity with LMOs, there should be a place for the consideration of benefits in the decision-making process, in particular in cases where it is necessary to decide how much risk (if any) is acceptable."

60. Several other submitters disagreed more directly with the assertion that there was a gap in guidance on benefit: One submitter cited Annex III of the Protocol, stating that Annex III only had provisions for risk assessment, and that benefits assessment was the domain of the decision-maker. The submitter concluded by stating that the inclusion of a benefits analysis in a risk assessment would conflate the roles of the risk assessor and the decision maker. The submitter further noted that benefit was far too intangible, with too many uncontrolled variables, so as to put it "out of the realm of the risk assessor". The submitter concluded that a benefits analysis cannot be included because there is no legislation to compel the realization of benefits.

61. Another submitter suggested that the examination of benefits assessment was being undertaken by the AHTEG and online Forum on socio-economic considerations. However, another submitter noted that not all benefits of an LMO fit into the socio-economic category, citing the example of an increase in biodiversity resulting from reduced pesticide use. The submitter stated that benefits are multi-dimensional

in the same way as risks. Another submitter spoke in reply about the opportunity cost of inaction in the absence of a benefits analysis, and how (and by whom) such a potential risk is assessed in the Cartagena Protocol framework, particularly if that risk/opportunity cost is not socioeconomic?

Perceived gaps on specific topics of risk assessment

62. Topics put forward as perceived assessment gaps within existing guidance:

(1) LMOs that are obtained through synthetic biology, including those with gene drives, and those obtained through genome editing or new plant breeding techniques;
(2) LM animals; particularly LM fish and aquatic organisms, and LM insects
(3) LM soil dwelling organisms
(4) LM birds
(5) Long-term environmental effects of LMO:
(6) LMOs obtained using RNA interference
(7) LM microorganisms and viruses, including those used in paratransgenesis
(8) Detection and identification of transgenes in landraces and wild relatives
(9) Open-field transfer of nucleic acids (either RNA or DNA) to plants and animals, eg, as biological pesticides
(10) LMOs involving the technique paratransgenesis[4]
(11) Centres and origins of genetic diversity
(12) Gene flow
(13) Genotype x environment interactions
(14) Conducting risk assessments where comparator organisms are not available
(15) Implementing "limits of concern"

63. Organisms obtained through synthetic biology (Perceived gap (1) above) were put forward by many submitters because "The rapid pace of development in synthetic biology means that existing risk assessment methodologies would need to be updated and adapted". Also, "Risk assessments of these organisms present new challenges when using the key factors that the guidance use as the basis for risk assessment of LMO which include; the lack of relevant and suitable comparators, development of an increasing number of traits in an organism developed through synthetic biology, the potential to use a number of novel techniques in development or modification of an organism with synthetic biology, and the difficulties in detecting the methods of modification that have been used." One submitter expressed concern that a risk as to how a risk assessment would even be done in the absence of a suitable comparator organism. The submitter went on to suggest the use of 'omics' technologies to fill this perceived gap. Another submitter suggested that technologies/methods like RNA interference and gene editing do not belong in the category of "synthetic biology". The submitter referred to a paper by Sauer et al., 2017 (See Appendix for reference) addressing the impracticality/challenges of 'omics techniques in the context of regulatory risk assessment, a view echoed by other submitters to the forum.

64. A submitter suggested that guidance on "LMOs developed with emerging synbio technologies such as dsRNA, gene editing, gene drives, and other new GM techniques that modify the epigenome" could be added to the AHTEG guidance. This was because of perceived issues to do with off-target effects, lack of suitable detection methods, identification of assessment endpoints, and suitable comparators. The submitter suggests an expansion of Section 1.5.1 on RNA interference.

65. Several submitters expressed perceived gaps in guidance regarding gene drives, due to their ability to alter population structures, and potentially cause the extinction of one or more species. International guidelines (e.g., regarding justifiable reasons for a release or mandatory integration of safety mechanisms) were seen to be of particular importance because of the potential for undesired transboundary movement.

4The use of LM symbiotic bacteria in disease vectors to express effector molecules inside the target vector to stop the transmission of the disease, rather than create LM disease vectors that do not transmit the disease.

66. The perceived gaps regarding LM fish (Perceived gap (2) above) pertain to their high mobility and the consequences of their contact or interbreeding with wild fish or conventional farmed fish, such as: "…out-competition of wild and conventional farmed fish of the same species and resulting trophic changes in the habitat as well as unexpected genetic changes in both the LMO and wild/farmed conventional relatives". Another submission suggested that guidance on LM fish "could consider eg, the specific life cycle characteristics of fish species, different uses of fish, different modification techniques and breeding strategies, data and research needs, and possible cumulative long-term effects." Another submitter suggested that adverse effects on wild salmon populations are already a problem due to escapes of non-GMO farmed salmon which may be worsened by escaped LM salmon. The submitter suggested that risk assessment guidance could include considerations on effects on genetic diversity, behaviour, mating success and survival success of their non-modified counterparts.

67. The perceived gaps to do with LM mosquitoes (Perceived gap (2) above) have to do with "…the potential adverse effects of unexpected releases of biting females, the potential rise of other disease vectors following suppression of the target species, wider effects on food webs and ecosystems in cases where there are drastic reductions in target populations, and survivability of LM insects with tetracycline-inducible systems in relation to potential environmental presence of tetracycline.

68. The perceived gap (3) in guidance on LM soil dwelling organisms was described as: considerations of eg, soil biodiversity, soil fertility and plant health. The submitter felt that guidance on the assessment of possible effects in highly variable ecosystems due to several abiotic factors.

69. The submitter perceived the gaps in guidance on LM birds (Perceived gap (4) above) as: the "…specific life cycle characteristics of birds, modification methods that are used for preserving birds and possible adverse effects to the ecosystem from such approaches, zoonosis issues, especially in relation to migratory bird species.

70. The perceived gap (5) in guidance on long-term effects of LMO: "There is a tendency that long-term effects, especially long-term indirect environmental effects and effects on non-target populations and abiotic factors are very superficial and often lack fundamental information".

71. Some submitters felt that the topics with perceived gaps simply are not covered or dealt with by other existing documents.

72. Another submitter suggested a peer-reviewed paper that discusses the utility of omics in risk assessment. Another submitter disagreed with this viewpoint, stating: "I don't think many of the techniques, especially 'omics' are yet mature enough to contribute substantially to the risk assessment framework."

Guidance on gene flow

73. One submitter suggested that the potential effect of LMOs on "geneflows" within genepools and its assessment as a perceived gap, along with the possibility that transgene flow within a species will jeopardize the existence of the species itself. The submitter recalled some experiments on the topic, but can't locate the information, and asked for help on the topic. Another submitter stated that extensive knowledge has been gathered on gene flow in the last 20 years, and provided several references on the topic (See Appendix). The submitter also stated that the potential consequences of gene flow has been the subject of risk assessments on a case-by case basis.

Guidance on all new topics

74. One submitter suggested that perhaps perceived gaps on benefits and on classes of organisms is worth addressing. However, another submitter expressed concern that improvements to risk assessments and capacity building cannot be made using a process that failed to deliver widely acceptable guidance after a very long process involving a great deal of human effort and a large number of AHTEGs and MOPs over more than 12 years. The submitter felt that the continued lack of definitions and criteria in this discussion will only result in more years of disagreement at an international level.

No perceived gaps in RA currently

75. Many submitters commented that they perceived no gaps in guidance regarding any LMOs. Two submitters noted that there have not been any perceived gaps identified at the level of the European Union, although as discussed above some EU member states have identified specific needs in their submissions to this forum

76. Other submitters stated that all LMOs developed, including organisms developed through recent technological advancements in synthetic biology, or organisms containing gene drive systems, can be comprehensively assessed based on available guidelines. The BCH was cited as a repository for many relevant guidelines (see Appendix for references). One submitter suggested that the current environmental risk assessment framework for LMOs is still valid for organisms that are in the current state of development of synthetic biology, and that close monitoring of scientific developments is necessary to see whether any existing risk assessment considerations or methodologies need to be adapted. Another submitter suggested that he wasn't aware of any synthetic biology organism being developed that has no relation to existing organisms and is intended to be used in a way for which there is no prior human experience. The submitter was careful to say that "…specific applications may require thoughtful application of guidance and prior experience – and potentially the collection of new information, to ensure that risk assessment is adequate to the task. But this will always be true, and there is no guidance document that will save us from the hard work of case by case risk assessment." Some submitters suggested that while risk assessment may become more complex (on a case-by-case basis) for some LMOs, there is still no gap in existing guidance materials on risk assessment. They reiterate that many existing guidance materials, including the AHTEG guidance are instructive in the fundamental methodology of conducting an environmental risk assessment on such organisms.

77. Another submitter commented that the operational definition of synthetic biology established by the AHTEG on Synthetic Biology in 2016 is not suitable to define any perceived gap in guidance, because the definition is too broad and includes most applications and techniques generally considered modern biotechnology prior to the advent of synthetic biology, including LMOs as originally defined in the Cartagena Protocol. As these can all be risk assessed with the methodologies in the Protocol, no gaps have been identified to date. Another submitter reiterates this point, noting that after several years of discussion under CBD, no one has identified exactly what is included under the term of "synthetic biology techniques". The AHTEG's definition of synthetic biology was considered by COP/MOP13 useful as a starting point, and not a final definition, for the purpose of facilitating scientific and technical deliberations under the Convention and its Protocols.

78. One submitter suggested that the document "Guidance on Uncertainty Analysis in Scientific Assessments", published in the EFSA Journal (see Appendix for reference) should be considered in discussions of Topic 3.

79. Another submitter reminded us that risk assessors are not just looking for differences or changes in genes or phenotypic traits, but rather for phenotypic traits in an LMO that are likely to result in adverse effects on the sustainable use of biological diversity, that is, a scientifically plausible risk hypothesis, or a realistic pathway to potential harm to the environment.

80. In addition to noting that there are no current perceived gaps in guidance, a submitter noted that "guidance" (whether existing or perceived to be required) cannot be the solution to every conceivable challenge in risk assessment, and that perceived "gaps" presented in this forum are just risk assessments for organisms or applications that have not yet been done, but which are not fundamentally different than risk assessments that have been done for similar organisms in the past.

81. Another submitter pointed out that risk assessment is not achieved through the choice of methodology but rather through ensuring the assessment is transparent with all inputs, assumptions, methods and results clearly described.

Access to training and resources

82. One submitter suggested that some may perceive gaps in guidance because the BCH search options are not user-friendly, and some resources are missing. She further suggests that some additional work is needed to make this important tool more useful to Parties and non-Parties alike.

83. One intervention focused on the thought that effort and resources should be directed toward training risk assessors to allow Parties to establish their biosafety frameworks, instead of creating additional documents for hypothetical hazards already covered by existing regulations. Other submitters reinforced this point, stating that limited experience in conducting risk assessment of LMOs is the biggest gap facing Parties, and the development of additional guidance documents will not solve this problem. Real time experience is required for Parties to come up with identified gaps based on their national priorities, needs and identified protection goals.

84. Another post suggested that if guidance is to be developed it should be directed toward the establishment of more generic guidance on the principles of risk assessment, risk management and monitoring and possibly on how to implement these principles to address specific cases. The submitter suggested that many of the perceived gaps mentioned in posts in this topic relate to the latter. The same submitter also noted that a strong reason not to develop new guidance on how to implement these principles that is too specific, is the timeframe necessary to develop such guidance documents. New techniques are emerging rapidly in the area of biotechnology. Internationally agreed specific guidelines can't be developed at an equally fast pace. Thus, any new species groups and techniques should be addressed within the existing framework and assistance on implementation of this framework to specific cases should be provided via other faster routes.

Process for establishing whether a gap exists and how to address it

85. Many submitters suggested that although they see no gaps in guidance currently, a clear process for evaluating perceived gaps and a set of criteria that must be fulfilled before considering whether additional guidance is necessary or that other methods of addressing the gap may be a better approach. If it is decided that further guidance on the specific guidance is deemed the best approach, it could then be decided who should write this guidance as to include the best expertise on the specific topic.

86. Several submitters suggested that a clear set of criteria needs to be agreed among the Parties of the Protocol before evaluating how any identified gaps should be addressed. One submitter suggested that the criteria proposed by the EU and its Member States in response to the CBD Notification 2017-035 (Risk Assessment and Risk Management) form a good basis for discussion among the Parties of the Protocol. In summary those criteria are:

(16) Risk assessment with regard to the topics in question is within the scope and objectives of the Protocol.
(17) Risk assessment with regard to the topics in question cannot be performed by using existing guidance documents.
(18) Specific topics with a high pace of scientific and technological advancement.
(19) Specific topics with potential adverse effects on biodiversity and/or human health.
(20) Specific topics might be prioritised if the LMOs in question are already, or are likely to be, commercialised and marketed somewhere in the world.

87. Criteria put forward by other submitters are:

(7) Emerging new challenges concerning risk assessment frameworks and methodologies, as well as concerning conservation and sustainable use of biological diversity, including new ways of exposure
(8) the topic is not too broad, and is well defined
(9) topic is identified by a Party of the Protocol

88. One intervention suggested that evidence based on scientific studies demonstrating that Annex III of the Protocol is not fully adequate for addressing identified risks, including the appropriate assessment

on environmental risk, must be shown before developing new guidance. Another submitter suggested that this will require very close monitoring of scientific developments.

89. In keeping with maintaining a solid scientific footing for the development of guidance on new topics (if any), another submitter pointed out that any new guidance material (assuming criteria are met) should only be written by experts and based on practical experience. This is necessary to produce a real and useful document rather than a theoretical, academic document.

90. A participant suggested that the SBSTTA be advised to make a list of the topics that have been suggested for additional guidance and compare that list with the list of available guidance resources to identify if there are any topics that are not adequately covered by existing guidance or guidance that is under development. If there are, the evidence should be presented as part of a case to enable the SBSTTA to propose criteria for prioritization of those remaining topics.

Appendix 1: References and links cited in the Jan/Feb 2018 BCH Online Forum for Risk Assessment and Risk Management:

Guidance documents:

Phytosanitary Measures (ISPMs) and their application to living modified organisms (LMOs) found at: https://www.ippc.int/static/media/uploads/ippc_ispmsforlmos_2016-02-24.pdf

IPPC Standards: https://www.ippc.int/en/core-activities/standards-setting/ispms/

EFSA guidance: https://www.efsa.europa.eu/en/applications/gmo/regulationsandguidance

OGTR (Australia) guidance: http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/risk-analysis-framework

Risk Assessment Guidance Listing (contains more than two dozen links and references to guidance documents): https://bch.cbd.int/cms/ui/forums/attachment.aspx?id=1467

Examples from the Risk Assessment Guidance Listing:

- Australia, Department of Health and Aging, Office of the Gene Technology Regulator. Risk Analysis Framework. May 2013. 139 pages. Available through: http://www.ogtr.gov.au . Guidelines for certification of containment conditions: http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/guidelines-1 Risk assessment reference documents: http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1
- Annex III of Cartagena Protocol, CODEX Principles for the Risk Analysis of Foods Derived from Modern Biotechnology: (http://www.oecd.org/science/biotrack/consensus-documents-safety-of-novel-foods-and-feeds.htm;
- OECD Consensus Documents: http://www.oecd.org/science/biotrack/consensusdocumentsfortheworkonharmonisationofregulatoryoversightinbiotechnology.htm
- AHTEG guidance: https://www.cbd.int/doc/meetings/bs/mop-08/official/bs-mop-08-08-add1-en.pdf
- Guidance on Uncertainty Analysis in Scientific Assessments". EFSA Journal http://dx.doi.org/10.2903/j.efsa.2018.5123
- Canada, Canadian Food Inspection Agency (CFIA) has been evaluating Plants with Novel Traits since 1996, http://www.inspection.gc.ca/plants/plants-with-novel-traits/eng/1300137887237/1300137939635 .
- Guidelines for Assessment of Novel Feeds: Plant Sources, http://www.inspection.gc.ca/animals/feeds/regulatory-guidance/rg-1/chapter-2/eng/1329298059609/1329298179464?chap=6, and Directive 94-08 revised (2004).

Assessment criteria for determining environmental safety of plants with novel traits at: http://www.inspection.gc.ca/plants/plants-with-novel-traits/applicants/directive-94-08/eng/1304475469806/1304475550733

- The CFIA – Plant BioSafety Office just released this update to Directive 94-08 last week, and it won't be in effect until June of 2018: http://inspection.gc.ca/plants/plants-with-novel-traits/applicants/directive-94-08-revised-/eng/1512588596097/1512588596818
- A link to the guidance document for Health Canada which also is part of the Canadian approval system can be found at: https://www.canada.ca/en/health-canada/services/food-nutrition/legislation-guidelines/guidance-documents/guidelines-safety-assessment-novel-foods-derived-plants-microorganisms/guidelines-safety-assessment-novel-foods-2006.html

Brazil risk assessment requirements: http://ctnbio.mcti.gov.br/resolucoes-normativas (in Portuguese)

A semi-quantitative approach to GMO risk-benefit analysis http://dx.doi.org/10.1007/s11248-010-9480-8 (paywall); Author's (free) copy: https://bch.cbd.int/cms/ui/forums/attachment.aspx?id=1465

Laboratory Biosafety and Biosecurity Risk Assessment Technical Guidance Document – Sandia National Labs 19JUN2017.pdf: https://bch.cbd.int/cms/ui/forums/attachment.aspx?id=1463

Review of 32 RA guidance documents: http://www.nature.com/nbt/journal/v35/n8/full/nbt.3926.html (paywall)

Risk assessments:

Australia: http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/ir-1

Japan: http://www.biodic.go.jp/bch/english/e_index.html

BCH: https://bch.cbd.int/database/riskassessments/ (mentioned in multiple posts – provided here for convenience)

Context

What do the 3rd National Reports and Results from testing tell us about the "Guidance on Risk Assessment of LMOs?: https://bch.cbd.int/cms/ui/forums/attachment.aspx?id=1466

BCH Roster of Experts: http://bch.cbd.int/database/experts/

Ethnobotany of Mexico: Interactions of People and Plants in Mesoamerica

http://www.springer.com/us/book/9781461466680 (reference was to Chapter 21 in the intervention)

IPPC Recommendation on LMOs, biosecurity and alien invasive species:

https://www.ippc.int/en/publications/84228/

Gene flow references:

1) https://vdf.ch/synthesis-and-overview-studies-to-evaluate-existing-research-and-knowledge-on-biological-issues-on-gm-plants-of-relevance-to-swiss-environments-1480741353.html?author_id=3362
2) https://ec.europa.eu/research/biosociety/pdf/a_decade_of_eu-funded_gmo_research.pdf
3) Ellstrand et al 2013 http://www.annualreviews.org/doi/full/10.1146/annurev-ecolsys-110512-135840
4) Ellstrand and Rieseberg 2016 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4947145/

Utility of 'omics' in RA:

1) https://lsspjournal.springeropen.com/articles/10.1186/s40504-017-0057-7

2) https://doi.org/10.1016/j.yrtph.2017.09.020

Training

ICGEB https://www.icgeb.org/ts-home.html

GenØK : http://genok.com/capacity-building/courses/

Appendix 2: Acronyms

ICGEB: International Centre for Genetic Engineering and Biotechnology

FAO: Food and Agriculture Organization of the United Nations

IPPC: International Plant Protection Convention

OIE: World Organisation for Animal Health

OGTR: The Office of the Gene Technology Regulator

ILSI: International Life Sciences Institute

WHO: World Health Organization

EFSA: European Food Safety Authority

OECD: The Organisation for Economic Co-operation and Development

AHTEG: Ad-Hoc Technical Expert Group

RARM: Risk Assessment and Risk Management

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