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Ad Hoc Technical Expert Group on Risk Assessment
First meeting
Montreal, Canada, 1–3 November 2023

Report of the Ad Hoc Technical Expert Group on Risk Assessment on its first meeting

Background

In its decision CP-10/10, the Conference of the Parties serving as the meeting of the Parties to the Cartagena Protocol on Biosafety established the Ad Hoc Technical Expert Group on Risk Assessment to develop additional voluntary guidance materials for conducting case-by-case risk assessments of living modified organisms containing engineered gene drives in accordance with annex III to the Protocol, with a specific focus on engineered gene drive mosquitoes. The Group was mandated to work on the basis of a detailed outline of additional guidance materials commissioned by the Executive Secretary. A draft outline of the materials was reviewed by the Online Forum on Risk Assessment and Risk Management. The Group was also mandated to analyse information submitted by Parties pursuant to paragraph 8 of decision CP-10/10, and, on that basis, to prepare a list of prioritized topics on which further guidance materials on risk assessment might be needed. A report of the work of the Group will be submitted for consideration by the Subsidiary Body on Scientific, Technical, and Technological Advice at its twenty-sixth meeting.

The first meeting of the Expert Group was attended by 19 experts from Parties, 1 expert from other Governments, 1 expert from indigenous peoples and local communities and 7 experts from observer organizations.

Item 1
Opening of the meeting

1. A representative of the Secretariat opened the meeting at 9 a.m. on 1 November 2023. The Acting Executive Secretary of the Convention on Biological Diversity, David Cooper, welcomed the experts to the meeting. He thanked the European Union for providing financial support for the organization of the meeting. He also expressed his gratitude to the Government of Finland for its contribution to the commissioning of the detailed outline of additional guidance materials on risk assessment of living modified organisms containing engineered gene drives.

Item 2
Organizational matters

2. The Ad Hoc Technical Expert Group on Risk Assessment elected Marja Ruohonen-Lehto as Chair of the meeting.

3. The Expert Group adopted the provisional agenda prepared by the Secretariat[1] with a modification in the order of items, as follows:

1. Opening of the meeting.
2. Organizational matters.
   (a) Election of officers;
   (b) Adoption of the agenda;
   (c) Organization of work.
3. Comments on the detailed outline of additional voluntary guidance materials to support the case-by-case risk assessment of living modified organisms containing engineered gene drives.
4. Review of the detailed outline:
   (a) Part A: risk assessment of living modified organisms containing engineered gene drive;
   (b) Part B: risk assessment of engineered gene drive *Anopheles* mosquitoes for malaria control.
5. Working modalities for the development of additional voluntary guidance materials.
6. List of prioritized topics for which further guidance materials on risk assessment may be needed.
7. Other matters.
8. Adoption of the report.
9. Closure of the meeting.

4. The Expert Group approved the provisional organization of work contained in annex I to the annotated provisional agenda.[2]

[1] CBD/CP/RA/AHTEG/2023/1/1.
[2] CBD/CP/RA/AHTEG/2023/1/1/Add.1/Rev.1.

Item 3
Comments on the detailed outline of additional voluntary guidance materials to support the case-by-case risk assessment of living modified organisms containing engineered gene drives

5. A representative of the Secretariat introduced the documents[3] related to agenda item 3 and provided an overview of the activities conducted in preparation for the meeting of the Expert Group.

6. The Expert Group agreed that it would work on the basis of the draft outline contained in document CBD/CP/RA/AHTEG/2023/1/3.

7. The Expert Group members noted that the outline provided useful information but that repetitions and duplication could be avoided by further streamlining the text and that sections that were not accurate should be revised.

8. The members were of the view that the information provided in the draft outline was too generic and that specific items identified in the Online Forum on Risk Assessment and Risk Management, the synthesis of submissions of information on risk assessment and the report of the Ad Hoc Technical Expert Group on its meeting held in 2020[4] were not adequately reflected. They mentioned some inaccuracies that would need to be addressed. There was also a problem with terminology and language, and some members suggested that priority should be given to the use of terminology from the Cartagena Protocol on Biosafety and from the Convention.

9. The members noted the need for further discussion on the species of mosquitoes that should be included in the additional voluntary guidance materials. They also noted advancements in risk assessment approaches, such as problem formulation, based on the construction of pathways to harm.

10. A few members highlighted the importance of Article 26 of the Protocol, on socioeconomic considerations, and noted that such considerations might be included in the decision-making process, while others mentioned that those considerations were not part of the risk assessment process. The members also stressed the importance of Article 23, on public awareness and participation, in particular the role of indigenous peoples and local communities, in the context of additional voluntary guidance.

11. The members provided input on the format and design of the draft outline. Several indicated their preference for a glossary of terms rather than the use of boxed illustrative examples and detailed definitions. They also said that all terms should contain citations to publications in which they are used and that unsupported claims should be avoided.

12. Lastly, some members pointed to the existence of relevant guidance materials developed by other international and regional processes.

Item 4
Review of the detailed outline

13. The Expert Group discussed part A of the detailed outline, as contained in document CBD/CP/RA/AHTEG/2023/1/3, which contained an overview of general considerations for the risk assessment of living modified organisms containing engineered gene drives. Following some initial discussions, the Chair established a friends of the Chair group, composed of two Expert Group members from each region, to work on the structure of part A of the additional voluntary guidance materials, on the basis of a problem formulation approach consistent with annex III to the Cartagena Protocol. The Friends of the Chair group met during the lunch period and reported back to the Expert Group.

[3] CBD/CP/RA/AHTEG/2023/1/2, CBD/CP/RA/AHTEG/2023/1/3, CBD/CP/RA/AHTEG/2023/1/INF/1 and CBD/CP/RA/AHTEG/2023/1/INF/2.

[4] CBD/CP/RA/AHTEG/2020/1/5.

14. After an exchange of views, the Expert Group agreed to work on the basis of the proposed structure presented by the Friends of the Chair group.

15. The Expert Group considered part B of the detailed outline, which provided an overview of general considerations for the risk assessment of living modified *Anopheles* containing an engineered gene drive for malaria control. Given the complexity of the matter, the diversity of mosquito species and potential applications in the near future, the Group discussed the focus and scope of its mandate in this regard.

16. In view of the limited time available to conclude its work, the Expert Group agreed that the focus of the guidance on engineered gene drive mosquitoes would be on vectors of human diseases. It noted that the guidance could also indicate potential applicability to situations involving mosquito vectors of non-human diseases.

17. The members considered whether or not to merge parts A and B of the draft detailed outline in order to streamline the text and remove redundancies and duplications. The Expert Group agreed to work on the basis of two separate parts that would be closely aligned and to revisit the issue of merging the two parts at its second meeting, once the text had been refined.

18. A revised draft outline of the additional voluntary guidance materials on risk assessment of living modified organisms containing engineered gene drives agreed upon by the Expert Group is provided in annex II.

19. The Expert Group held extensive discussions on the content of the various sections of the draft outline. A general summary of points raised during the discussions, including suggestions made by the members, and specific considerations to be taken into account for the further drafting of the additional voluntary guidance materials are contained in annex III.

Item 5
Working modalities for the development of additional voluntary guidance material

20. The Expert Group discussed how to organize its future work for developing the additional voluntary guidance materials. It agreed to establish five drafting groups to work on separate components contained in the additional voluntary guidance. The groups were divided as follows:

(a) Group A: sections 1–6 of the draft outline;

(b) Group B: mosquitoes;

(c) Group C: related issues;

(d) Group D: monitoring;

(e) Group E: glossary of terms.

21. The Chair appointed chairs to lead each group. Members were assigned to each group, ensuring regional balance for groups A to D, with one expert overseeing the glossary of terms (see annex IV for the group membership).

Item 6
List of prioritized topics for which further guidance materials on risk assessment may be needed

22. A representative of the Secretariat introduced agenda item 6. He presented an overview of the process undertaken for compiling the list of prioritized topics for which further guidance materials on risk assessment might be needed.

23. The members took note of the following three submissions:

(a) Guidance materials are needed on living modified organisms containing engineered gene drives;

(b) Guidance materials are needed on living modified aquatic organisms, including algae, crustaceans and fish;

(c) No further guidance materials on risk assessments are required.

24. Some members suggested that the limited number of submissions received indicated that there was no urgent need for additional topics to be considered for further guidance materials on risk assessment. Given the low number of submissions, it was agreed that an additional request for submissions might be required before the second meeting of the Expert Group.

25. With respect to decision CP-10/10, the members noted that the topic of risk assessment of living modified fish would be considered by the Conference of the Parties serving as the meeting of the Parties to the Protocol at its eleventh meeting.

26. It was also noted that the topic of risk assessment of living modified organisms containing engineered gene drives was being addressed by the current Expert Group.

Item 7
Other matters

27. The Expert Group agreed to hold its second meeting in February or early March 2024, at which it would discuss the materials elaborated by the drafting groups, finalize the list of prioritized topics and draft recommendations for submission at the twenty-sixth meeting of the Subsidiary Body on Scientific, Technical and Technological Advice. A concern was however raised regarding the very short time to conclude those tasks in a timely manner.

Item 8
Adoption of the report

28. The Chair presented the draft report of the meeting, which was adopted, as orally amended.

Item 9
Closure of the meeting

29. Following the customary exchange of courtesies, the meeting was closed at 12 a.m. on 4 November 2023.

Annex I

List of participants

A. Experts nominated by Parties

Belarus
Galina Mozgova
Head, National Coordination Biosafety Centre
Institute of Genetics and Cytology, National Academy of Sciences

Bosnia and Herzegovina
Adaleta Durmić-Pašić
Scientific Advisor, Head of the Genetically Modified Organisms and Food Safety Laboratory
Institute of Genetic Engineering and Biotechnology, University of Sarajevo

Brazil
Luciana Pimenta Ambrozevicius
Federal Agricultural Inspector
Ministry of Agriculture and Livestock

Burkina Faso
Mathurin Wend-rabo Rouamba
Biosafety Officer
Agence nationale de biosécurité

Cambodia
Monyrak Meng
Deputy Director General
Ministry of Environment

China
Bao-Rong Lu
Professor
Fudan University

Colombia
Gabriel Mutis Namur
Biotechnology Regulatory Affairs Leader
National Institute for Food and Drug Surveillance

Cuba
Marvis Esther Suárez Romero
Senior Specialist in Regulation, Control and Safety
Office of Regulation and Environmental Safety, Environmental Control Directorate

Ecuador
Maria de Lourdes Torres
Coordinator and Professor, Biotechnology
Universidad San Francisco de Quito

European Union
Yann Devos
Senior Scientific Officer
European Food Safety Authority

Finland
Marja Ruohonen-Lehto
Senior Adviser
Director General's Office/Authority Services
Finnish Environment Institute

France
Christophe Boëte
Researcher
Institut de recherche pour le développement

Germany
Werner Schenkel
Scientific Officer
Federal Office of Consumer Protection and Food Safety

Malaysia
Kumitaa Theva Das
Senior Lecturer
Universiti Sains Malaysia

Nigeria
Josephine Ejile Amedu
Assistant Chief Scientific Officer
National Biosafety Management Agency

Philippines
Barbara L. Caoili
Professor
University of the Philippines Los Baños College

Republic of Moldova
Angela Lozan
Project Manager, National Office of Environmental Projects Implementation
Ministry of Environment

Slovenia
Ruth Rupreht
Senior Advisor, Biotechnology Section
Ministry of the Environment, Climate and Energy

Tunisia
Raja Chalghoumi
Associate Professor
University of Carthage

B. Experts nominated by other Governments

United States of America

Kayla Knilans
Scientific Policy Advisor
United States Department of Agriculture

C. Experts nominated by indigenous peoples and local communities

Society for Wetland Biodiversity Conservation Nepal

Kamal Kumar Rai
Chair, Research, Conservation and Advocacy

D. Experts nominated by organizations

CSIRO Data61

Keith Hayes
Team Leader and Senior Research Scientist

Foundation for the National Institutes of Health

Brinda Dass
Senior Technical Expert, Policy Lead Gene Drive Research

European Network of Scientists for Social and Environmental Responsibility

Nicolas Defarge
Researcher, Molecular Biologist

Third World Network

Eva Sirinathsinghji
Research Associate

Global Industry Coalition

Felicity Keiper
Global Regulatory Policy Manager, Seeds and Traits
BASF Australia

Federation of German Scientists

Ricarda Steinbrecher
Working Group on Agriculture and Biodiversity, including Biotechnology

Imperial College London

John Connolly
Senior Regulatory Science Office

E. United Nations Environment Programme

Alex Owusu-Biney
United Nations Environment Programme-Global Environment Facility Biosafety Portfolio of Projects

F. Secretariat of the Convention on Biological Diversity

Wadzanayi Mandivenyi
Senior Programme Management Officer
Head, Biosafety Unit

Austein McLoughlin
Associate Programme Management Officer
Biosafety Unit

Melissa Willey
Programme Management Assistant
Biosafety Unit

Ashley Bastiansz
Independent Contractor
Biosafety Unit

Anastasia Beliaeva
Programme Management Assistant
Biosafety Unit

Paola Scarone
Senior Programme Management Assistant
Biosafety Unit

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Independent Contractor
Biosafety Unit

Annex II

Revised draft outline of the additional voluntary guidance materials on risk assessment of living modified organisms containing engineered gene drives

1. Introduction
    - 1.1 Objective
    - 1.2 Establishing the context and scope
2. Making policy protection goals operational
    - 2.1 Determination of assessment endpoints
    - 2.2 Identification of measurement endpoints
3. Problem formulation
    - 3.1 Identification of potential adverse effects on the assessment endpoints
    - 3.2 Devising plausible pathways to harm or adverse outcome pathways
        - 3.2.1 Identification of any novel genotypic and phenotypic characteristics associated with living modified organisms containing engineered gene drives that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health
        - 3.2.2 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
        - 3.2.3 Evaluation of the consequences should these adverse effects be realized
    - 3.3 Formulation of risk hypotheses
4. Test risk hypotheses to characterize overall risks
    - 4.1 Quality and relevance of information
    - 4.2 Choice of comparators
    - 4.3 Identification of uncertainty
        - 4.3.1 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 (case-specific, tiered, stepwise, familiarity, data reliability and weight-of-evidence approach)
5. Recommendations of acceptability of risk and identification of risk management strategies
    - 5.1 Consideration of uncertainty
        - 5.1.1 Recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage those risks
6. Proposing risk management options
    - 6.1 Consideration of uncertainty
        - 6.1.1 Appropriate risk management and/or monitoring strategies
7. Related issues

Glossary

Annex III

Considerations for drafting additional voluntary guidance materials

Overarching elements

- There was agreement to work on the basis of section A of the detailed outline as a starting point; however, further textual refinement was needed, including the removal of redundant and repetitive text.
- The detailed outline was considered too similar to guidance for conventional living modified organisms and not specific enough for living modified organisms containing engineered gene drives. The need for further clarification of the differences between conventional living modified organisms and living modified organisms containing engineered gene drives should be emphasized.
- It was agreed to proceed on the basis of the content related to both living modified organisms containing engineered gene drives and living modified mosquitoes containing engineered gene drives.
- It was agreed that the focus of the guidance on engineered gene drive mosquitoes would be on vectors of human diseases.
- It was noted that the guidance could also indicate its potential applicability to situations involving mosquito vectors of non-human diseases.
- It was agreed to consider improving the readability of the final document with the use of text boxes, tables and figures, among others.
- The structure of the document was re-organized, as described in annex II. The additional voluntary guidance materials would use a problem formulation approach based on the construction of pathways to harm.
- Terminology in the document should be standardized and based on existing publications, and reflect language used in the Cartagena Protocol on Biosafety and the Convention on Biological Diversity. A glossary would be developed.

Section 1. Objective and scope of the additional voluntary guidance materials

- It was agreed that section 1 would be further refined to include the following elements:
  - Clarity on the target audience of the guidance as being the Parties to the Cartegena Protocol
  - Indication of which mosquito taxa in the family Culicidae should be included in the scope
- It was noted that the detailed outline followed the structure of the road map (2016), containing repetitive and generic text, and it was decided that the work of the Expert Group would be based on a new structure, as contained in annex II.
- The new proposed structure was aligned with annex III to the Cartagena Protocol
- Reference should be made to the report of the Ad Hoc Technical Expert Group on Risk Assessment on its meeting held in 2020 and to the summary of discussions held in the meetings of the Open-ended Online Forum on Risk Assessment.[5]

[5] CBD/CP/RA/AHTEG/2020/1/5 and CBD/CP/RA/AHTEG/2023/1/INF/1, respectively.

Part A: risk assessment of living modified organisms containing engineered gene drives

Points raised under each section are summarized below.

Section 2. Introduction

- Incorporate general information on engineered gene drives, including text from section 3.
- Further elaborate on engineered gene drive elements and concepts, using, for example, the Guidance Framework for Testing Genetically Modified Mosquitoes (World Health Organization, 2021), temporal characteristics, spatial characteristics, combination, persistence and spread.
- Consider definitions and classes of engineered gene drives and the potential for unintended behaviour.

Section 3. Overarching issues in the risk assessment process on living modified organisms containing engineered gene drives

- Include a new section to outline specific challenges to risk assessment and management methodology with living modified organisms containing engineered gene drives, taking into account document CBD/CP/RA/AHTEG/2020/1/5.
- Consider alternative public participation approaches complementary to consultative meetings.
- Consider inclusive public participation to include the perspectives of indigenous peoples and local communities.
- Section 3.2. Quality and relevance of information:
  - Swap the order of 3.2.1 (criteria for the quality of scientific information) and 3.2.2 (sources and relevance of information for the risk assessment)
  - Include a weight-of-evidence approach and consider the European Food Safety Authority guidance
- Section 3.3. Identification and consideration of uncertainty:
  - Specifically mention the precautionary approach
  - Incorporate other relevant scientific publications (e.g. from the World Health Organization and the European Food Safety Authority) related to the determination of scientific uncertainty
  - Use categories of uncertainty (epistemic, variability and linguistic)
  - Consider the benefits and limitations of modelling
  - Consider the feasibility of potential application of cut-off criteria, as appropriate

Section 4. Planning phase of the risk assessment of living modified organisms containing engineered gene drives

- Reconsider the list of items (i) to (xii) and their placement in the appropriate section of the document, with the possibility of deleting items, as appropriate.
- With regard to stakeholder engagement:
  - Consider text placement and prominence in the appropriate section of the document
  - Ensure the full and effective participation of indigenous peoples and local communities, including social and cultural considerations (see Cartagena Protocol, Article 26, on socioeconomic considerations)

- Consider appropriate and effective modalities for public participation, including, where appropriate, reference to Article 23, on public awareness and participation, of the Cartagena Protocol.

- Section 4.3. Choice of comparators:
  - Clarify comparators at the genetic and environmental levels
  - Further consider sibling species, species complexes and the potential for hybridization
  - Consider the use of multiple comparators, such as insecticides, *Wolbachia*, related living modified organisms and integrated pest management, while considering their utility and limitations
  - Refer to document CBD/CP/RA/AHTEG/2020/1/5 regarding potential difficulties in establishing baselines and comparators

Section 5. Conducting the risk assessment

- Consider the categorization of unintended effects in the European Food Safety Authority guidance on the environmental risk assessment of genetically modified animals of 2013.
- Further clarify the understanding of the recommendation of risk acceptability in step 5.
- Section 5.1. Step 1: identification of any novel genotypic and phenotypic characteristics associated with the living modified organisms containing engineered gene drives that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health:
  - Illustrative examples will need further elaboration, including re-formulation, moving the text to a more appropriate section of the document and consider instead the use of "real life" examples, as appropriate
  - Clearer focus should be placed on elements related to living modified organisms containing engineered gene drives, such as pathogens, pathogen evolution, population dynamics of other species in the receiving environment and next-generation effects
  - Existing guidance documents should be considered to complement the text
  - A table with plausible pathways could be used to inform the process
  - A figure could be included that depicts multiples releases of living modified organisms containing engineered gene drives, multiple types of engineered gene drives and alternative mechanisms (e.g. split drives)
- Section 5.2. Step 2: 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:
  - Include information on how to analyse exposure quantitatively
  - Refine text related to mitigation measures due to persistence
  - Consider mitigation strategies and their limitations
  - Consider the instability of engineered gene drive systems (e.g. the unexpected disappearance of the transgene function)
  - Consider using diagrams to describe exposure characterization (e.g. risk matrix)
  - Clarify certain terms (e.g. population suppression, population replacement, population modification and correct the terms "species suppression" and "species replacement")
  - Refer to document CBD/CP/RA/AHTEG/2020/1/5
  - Consider the *Guidance framework for Testing Genetically Modified Mosquitoes* and *Gene Drives: Pursuing Opportunities, Minimizing Risk* (Center for Health Security, Johns Hopkins University, 2020)
- Section 5.3. Step 3: evaluation of the consequences should these adverse effects be realised:
  - Provide information on how to analyse consequences quantitatively

- Refine text related to hazard characterization (e.g. placement, use of examples for the environment, human health and animal health)
- Consider irreversibility, as appropriate

- Section 5.4. Step 4: 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:
  - Include quantitative examples
- Section 5.5. Step 5: recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage those risks:
  - Include the precautionary approach
  - Mention uncertainty in relation to scientific benefit analyses
  - Understand problem formulation as part of an iterative process
  - Refer to guidelines related to indigenous peoples and local communities

Section 6. Related issues

- Identification of complementary concepts to the risk assessment component versus identification of concepts for the decision-making process.
- Relation to the type of living modified organisms containing engineered gene drives (e.g. population replacement versus population suppression).
- Addressing socioeconomic (see Cartegena Protocol, Article 26), cultural and ethical considerations, including specific guidelines for indigenous peoples and local communities.
- Appropriate risk benefit analysis elements.
- Consideration of benefits for human health as described in the *Guidance Framework for Testing Genetically Modified Mosquitoes*.
- Consideration of document CBD/CP/RA/AHTEG/2020/1/5.
- Consideration of confidential business information (e.g. Cartagena Protocol, Article 21, on confidential information), decision-making, liability and redress elements.
- Inclusion of public awareness, education, public participation (e.g. full and effective participation of indigenous peoples and local communities), access to information and risk communication.
- Comparisons of novel strategies with alternative interventions, current measures and cost of inaction.
- Considering potential for long-term hazards and possible hazards for future generations, non-target species and human health.
- Considering reviewing the risk assessment process.
- Consideration of transboundary movements (see Cartagena Protocol, Article 17, on unintentional transboundary movements and emergency measures).
- The multidisciplinary Ad Hoc Technical Expert Group on Synthetic Biology to Support the Process for Broad and Regular Horizon Scanning, Monitoring and Assessment was mentioned during discussions.

Part b: risk assessment of living modified *Anopheles* containing an engineered gene drive for human disease control

Section 7. Introduction

- Agree to replace "*Anopheles"* with "mosquitoes" on vectors of human diseases.
- Agree to have "risk assessment considerations for" in the title for part B.
- Consider the inclusion of a definition of the mosquito taxon Culicidae.
- Clarify the terminology utilized for living modified mosquitoes containing engineered gene drives.
- Further elaborate on the biological, environmental, human health and epidemiological aspects related to mosquitoes.
- Correct information related to the type of releases of living modified mosquitoes containing engineered gene drives.
- Refer to document CBD/CP/RA/AHTEG/2020/1/4, a study on risk assessment: application of annex I to decision CP-9/13 to living modified organisms containing engineered gene drives.
- Consider the *Guidance Framework for Testing Genetically Modified Mosquitoes*.

Section 8. Objective and scope

- No comments were received.

Section 9. Planning phase of the risk assessment of engineered gene drives in *Anopheles*

- Further development of section 9 beyond comparators.
- Section 9.1. Choice of comparators:
  - The choice of comparators should be related to the risk hypotheses and the specific engineered gene drives (e.g. engineered gene drives for population suppression versus population modification)
  - There should be a broad use of comparators, including current practices, and of multiple comparators
  - When considering the choice of comparators, they should be related not only to the efficacy but also to impacts on the environment
  - Further consideration comparators are needed to avoid measurements of the efficacy of the engineered gene drive
  - Reference should be made to document CBD/CP/RA/AHTEG/2020/1/5 in relation to the difficulties in choosing appropriate comparators.

Section 10. Conducting the risk assessment of living modified *Anopheles* containing an engineered gene drive

- Improvement of the content in section 10.
- Section 10.1. Step 1. Characterization of the living modified mosquito containing an engineered gene drive:
  - Re-organize the section to start with ecological and biodiversity-related considerations
  - Consider target species in terms of sibling species and species complexes, as appropriate
  - Give further consideration to health (e.g. in relation to pathogens)
- Section 10.2. Step 2. Unintended effects on biological diversity (species, habitats, ecosystems and ecosystem function and services):

- It is important to explain differences between conventional living modified organisms and living modified organisms containing engineered gene drives (e.g. preferential inheritance and spatio-temporal scale)
- Clarify text in subsections on vertical and horizontal gene transfer
- Potentially include quantitative information related to horizonal gene transfer.

- Section 10.2.3 (*Persistence of the transgene in the ecosystem*):
  - Replace "species suppression" with "population suppression"
  - Include information on a tiered approach
  - Consider the *Guidance Framework for Testing Genetically Modified Mosquitoes*
- Section 10.2.4. (*Evolutionary response*):
  - Refine text, clarify the use of terminology (e.g. selection pressure) and provide improved context for this subsection
  - Possibility to include modelling information and quantitative estimate related to pathogen virulence in host
  - Include information on pathogen evolution in response to the release of living modified mosquitoes containing engineered gene drives
- Section 10.2.5 (*Unintentional transboundary movements*):
  - Opportunity to use modelling.
  - Previous experience with other living modified mosquitoes and *Wolbachia* could provide insights.
  - Could be moved to content related to section 6 (*Related issues*)
  - Reference to Article 17 of the Cartagena Protocol
  - Potential new section 10.2.6 (Mode of transport)
- Section 10.3. Steps 4 and 5. Risk management strategies:
  - This section was not discussed during the meeting of the Expert Group.
  - It was noted that the section contained text repetitive and redundant with sections 5.4 and 5.5 in part A of the detailed outline

Section 11. Monitoring living modified *Anopheles* containing engineered gene drives released in the environment

- This section was not discussed during the meeting of the Expert Group.
- It was noted that the section contained text repetitive and redundant with section 5.2 in part A of the detailed outline.
- The text below comes from discussions related to monitoring under part A:
  - Case-specific/hypothesis-driven monitoring versus general surveillance, including designation of responsibility
  - Potential to measure consequences quantitatively
  - Feasibility of monitoring in consideration of national circumstances, funding and capacity
  - Determination of monitoring based on the outcome of the risk assessment process
  - Monitoring living modified organisms containing engineered gene drives in relation to challenges to baselines and existing monitoring frameworks.
  - Engagement of indigenous peoples and local communities in monitoring
  - Refer to document CBD/CP/RA/AHTEG/2020/1/5

Glossary

- The glossary should contain all terms used in the additional voluntary guidance materials.

- All terms in the glossary should contain citations to publications in which they are used.

Tracking of sections between the detailed outline and the proposed structure for the additional voluntary guidance materials

Section of the proposed structure for the additional voluntary guidance materials	*Section of the detailed outline*
1. **Introduction** 1.1. Objective 1.2. Establishing context and scope	1. Objective and scope of the additional voluntary guidance materials 2. Introduction 4.1. Establishing the context and scope
2. **Making policy protection goals operational** 2.1. Determination of assessment endpoints 2.2. Identification of measurement endpoints	3.1. Protection goals, assessment end points and measurement end points
3. **Problem formulation** 3.1. Identification of potential adverse effects on the assessment endpoints 3.2. Devise plausible pathways to harm or adverse outcome pathways 3.2.1. Identification of any novel genotypic and phenotypic characteristics associated with the living modified organisms containing engineered gene drives that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health 3.2.2. 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 3.2.3. Evaluation of the consequences should these adverse effects be realized 3.2.4. Rationale 3.3. Formulation of risk hypotheses	4.2. Problem formulation 5.1. Step 1. Identification of any novel genotypic and phenotypic characteristics associated with the living modified organisms containing engineered gene drives that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health 5.2. Step 2. 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 5.3. Step 3. Evaluation of the consequences should these adverse effects be realized

Section of the proposed structure for the additional voluntary guidance materials	*Section of the detailed outline*
4. **Test risk hypotheses to characterize overall risks** 4.1. Quality and relevance of information 4.2. Choice of comparators 4.3. Identification of uncertainty 4.3.1. 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 (case-specific, tiered, stepwise, familiarity, data reliability and weight-of-evidence approach)	3.2. Quality and relevance of information 3.3. Identification and consideration of uncertainty 4.3. Choice of comparators 5.4. Step 4. 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
5. **Recommendation of acceptability of risk and identification of risk management strategies** 5.1. Consideration of uncertainty 5.1.1. Recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage those risks	5.5. Step 5. Recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage those risks
6. **Propose risk management options** 6.1. Consideration of uncertainty 6.1.1. Appropriate risk management and/or monitoring strategies	5.5. Step 5. Recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage those risks 11. Monitoring living modified *Anopheles* containing engineered gene drives released in the environment
7. **Related issues**	6. Related issues
Glossary	–

Annex IV

Drafting groups

Group	*Revised draft outline*	*Proposed composition*
A	Part A 1. Introduction 2. Making policy protection goals operational 3. Problem formulation 4. Test risk hypotheses to characterize overall risks 5. Recommendation of acceptability of risk and identification of risk management strategies 6. Propose risk management options	**Chair**: Werner Schenkel Raja Chalghoumi Monyrak Meng Ruth Rupreht Luciana Pimenta Ambrozevicius Yann Devos Kayla Knilans Ricarda Steinbrecher Keith Hayes
B	Part B Mosquitoes	**Chair**: Barbara L. Caoili Mathurin Wend-rabo Rouamba Kumitaa Theva Das Galina Mozgova Marvis Esther Suárez Romero Christophe Boëte Eva Sirinathsinghji John Connolly
C	Related issues	**Chair**: Angela Lozan Kamal Kumar Rai Lilian Chimphepo Adaleta Durmić-Pašić Gabriel Mutis Namur Nicolas Defarge
D	Monitoring	**Chair**: Josephine Ejile Amedu Maria de Lourdes Torres Bao-Rong Lu Brinda Dass
E	Glossary	Felicity Keiper