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AD HOC TECHNICAL EXPERT GROUP ON SYNTHETIC BIOLOGY

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Item 3 of the provisional agenda*

OVERVIEW OF WORK DONE IN RESPONSE TO DECISION XIII/17 AND BACKGROUND INFORMATION TO FACILITATE DELIBERATIONS BY THE AD HOC TECHNICAL EXPERT GROUP ON SYNTHETIC BIOLOGY

I. INTRODUCTION

1. In [decision XIII/17](#), paragraph 11, the Conference of the Parties to the Convention on Biological Diversity decided to extend the mandate of the Ad Hoc Technical Expert Group on Synthetic Biology in accordance with the terms of reference annexed to the decision and also to contribute to the completion of the assessment pursuant to [decision XII/24](#), paragraph 2.

2. The Conference of the Parties also decided to extend the open-ended online forum to support the work of the Ad Hoc Technical Expert Group on Synthetic Biology, and invited Parties, other Governments, indigenous peoples and local communities and relevant organizations to continue nominating experts to take part in the open-ended online forum.

3. In paragraph 10 of the same decision, the Conference of the Parties also invited Parties, other Governments, relevant organizations and indigenous peoples and local communities to submit to the Executive Secretary information and supporting documentation on:

(a) Research on the benefits and adverse effects of organisms, components and products¹ of synthetic biology on biodiversity; public and multi-stakeholder dialogues and awareness-raising activities; and cooperation in the development of guidance and capacity-building activities noted in paragraph 9 of the decision;

(b) Evidence of benefits and adverse effects of synthetic biology vis-à-vis the three objectives of the Convention;

(c) Experiences in conducting risk assessments of organisms, components and products of synthetic biology, including any challenges encountered, lessons learned and implications for risk assessment frameworks;

* CBD/SYNBIO/AHTEG/2017/1/1.

¹ For the purpose of the present note and in accordance with the report of the previous meeting of the AHTEG, to facilitate a common understanding in the discussions on similarities and differences with LMOs, the term “components” is used to refer to parts used in a process (e.g. a naked DNA molecule), and “products” as the output of a process (e.g. a chemical fragrance).

(d) Examples of risk management and other measures that have been put in place to avoid or minimize the potential adverse effects of organisms, components and products of synthetic biology, including experiences of safe use and best practices for the safe handling of organisms developed through synthetic biology;

(e) Regulations, policies and guidelines in place or under development which are directly relevant to synthetic biology;

(f) Knowledge, experience and perspectives of indigenous peoples and local communities in the context of living in harmony with nature for comparison and better understanding of the potential benefits and adverse effects of synthetic biology.

4. Pursuant to the decision, the Executive Secretary established a process comprising: (a) the submission of information on synthetic biology; (b) an open-ended online forum with online discussions on specific topics of synthetic biology; (c) one face-to-face meeting of the Ad Hoc Technical Expert Group; and (d) peer review of the outcomes of the process. The outcomes of this process will be submitted for consideration by the Subsidiary Body on Scientific, Technical and Technological Advice at its twenty-second meeting, scheduled to be held in Montreal, Canada, from 2 to 7 July 2018.

5. Regarding the composition of the Ad Hoc Technical Expert Group, following informal consultations by the Secretariat, it was determined that a number of experts were no longer available to serve as members of the Group. Thus, in accordance with the consolidated modus operandi of the Subsidiary Body on Scientific, Technical and Technological Advice and the approval of its Bureau, the Secretariat selected new members from among the experts nominated by Parties. The selection was made on the basis of their expertise, taking into account geographic and gender balance as well as participation in the discussions of the Online Forum on Synthetic Biology. The Secretariat also identified experts nominated by other Governments, indigenous peoples and local communities, and relevant organizations to serve as observers in the Group.

6. The purpose of the present document is to facilitate the deliberations of the Ad Hoc Technical Expert Group at its meeting from 5 to 8 December 2017. Section II provides a synthesis of views submitted in response to paragraph 10 of decision XIII/17; section III presents a synthesis of the discussions carried out under the open-ended online forum; section IV contains an overview of other relevant processes under the convention and its protocols; and section V contains conclusions for consideration by the Ad Hoc Technical Expert Group.

II. SYNTHESIS OF VIEWS IN RESPONSE TO PARAGRAPH 10 OF DECISION XIII/17

7. In response to decision XIII/17, paragraph 10, the Executive Secretary issued a notification on 16 March 2017 inviting Parties, other Governments, relevant organizations and indigenous peoples and local communities to submit information and supporting documentation on the topics referred to in the decision.

8. A total of 29 submissions² were received by the Secretariat. Among the submissions, 15 were from Parties,³ 1 from a non-Party,⁴ and 13 from organizations.⁵

² The notification and submissions are available online at <http://bch.cbd.int/synbio/submissions/2017-2018.shtml>.

³ Australia, Brazil, Bulgaria, Canada, Colombia, Democratic Republic of the Congo, European Union, Finland, France, India, Iraq, Mexico, New Zealand, South Africa, and United Kingdom of Great Britain and Northern Ireland.

⁴ United States of America

9. Furthermore, several submissions cited or included electronic copies of documents which have already been published elsewhere. A list of such documents is available in annex I to document [CBD/SYNBIO/AHTEG/2017/1/INF/1](http://www.biosintetica.mx/CBD/SYNBIO/AHTEG/2017/1/INF/1).

A. Research, cooperation and activities

10. In describing their involvement in research, cooperation and activities, some Parties, other Governments and relevant organizations indicated that they support the undertaking of research on synthetic biology in their countries and in some cases do so through the provision of funds to the relevant research groups. One Party also indicated that it has a database on synthetic biology projects that it is carrying out.⁶

11. Several Parties described the existence of specialized scientific committees, panels and advisory boards that focus on multidisciplinary research on various aspects of synthetic biology ranging from assessing the scientific and technical impacts of synthetic biology to researching social, ethical, regulatory, and legal issues related to synthetic biology. Moreover, some of these committees are also responsible for holding awareness-raising activities, such as publishing reports, information notes and hosting and participating in seminars in order to encourage public and multi-stakeholder dialogues on the potential benefits and potential adverse effects of organisms, components and products of synthetic biology on biodiversity.

12. In contrast, other Parties indicated that they have limited or no capacity to carry out synthetic biology research. Some Parties also indicated that they make an effort to stay abreast of developments that occur in the field of synthetic biology through regional cooperation and participation in trainings and workshops focusing on synthetic biology.

B. Evidence of benefits and adverse effects of synthetic biology

13. Some submissions recalled the potential of synthetic biology to develop efficient and effective ways to respond to challenges associated with bioenergy, agriculture, health and chemical production, amongst other applications. Some submissions also noted that the same applications may have adverse effects on biodiversity through invasiveness, persistence, unintended effects caused by accidental introduction into the environment and the potential consequences as a result of altering natural populations.

14. Some submissions, on the other hand, did not provide examples of benefits and adverse effects of synthetic biology vis-à-vis the three objectives of the Convention but, rather, noted that the benefits and adverse effects of synthetic biology are to be considered on a case-by-case basis using robust risk assessment methodology and implementing sound risk management procedures.

C. Experiences in conducting risk assessments of organisms, components and products of synthetic biology

15. In describing their experiences in conducting risk assessments of organisms, components and products of synthetic biology, including any challenges encountered, lessons learned and implications for risk assessment frameworks, some Parties, one non-Party and several organizations noted that existing

⁵ Biofuelwatch, Centre for the Study of Science and Innovation Policy, European Network of Scientists for Social and Environmental Responsibility, Federation of German Scientists, GenØk - Centre for Biosafety, Global Industry Coalition, Imperial College London, Island Conservation, North Carolina State University, Sustainability Council of New Zealand, The World Conservation Union – IUCN, Third World Network, University of Bristol.

⁶ <http://www.biosintetica.mx/>

risk assessment methodologies have been successfully applied in conducting risk assessments of living modified organisms for several years. They also indicated that, in the past, as organisms became more complex with advances in modern biotechnology, adaptations were made to existing risk assessment frameworks in order to perform an adequate risk assessment. They therefore noted that such an approach could be applied to assess the risk from organisms developed through synthetic biology.

16. Some Parties and several organizations noted, however, that synthetic biology poses specific challenges and that existing risk assessment methodologies, which are based on more traditional techniques of modern biotechnology, cannot be adequately applied to organisms developed through synthetic biology. Gaps identified include: (a) the absence of suitable comparators;; (b) a greater depth of intervention, leading to the presence of multiple modifications which may interact in unknown ways, resulting in unexpected outcomes; (c) the accelerated rate of developing organisms using synthetic biology; and (d) off-target changes to the genome caused by genome editing tools. These gaps, among others, may pose challenges to regulatory systems in implementing current risk assessment methodologies. Thus, there may be a need for additional research, and the development of revised risk assessment frameworks, to address the gaps.

D. Examples of risk management and other measures

17. With regard to examples of risk management and other measures that have been put in place to avoid or minimize the potential adverse effects of organisms, components and products of synthetic biology, including experiences of safe use and best practices for the safe handling of organisms developed through synthetic biology, some Parties listed several avenues through which this is being achieved.

18. With respect to living modified organisms (LMOs) that are intended for release into the environment, some countries indicated that their existing biosafety legislations, which also apply to organisms developed through synthetic biology, establish specific conditions which must be met and approved by the competent national authorities prior to the release of any such organisms. In addition, a monitoring plan should be put in place prior to the release. Furthermore, monitoring plans may include inspection measures and the use of testing methods to detect unauthorized LMOs that have been released into the environment.

19. With regard to organisms developed through synthetic biology that are intended for contained use, some countries indicated that their existing biosafety legislation set out specific containment guidelines for LMOs. These guidelines outline the varying levels of containment that are required when handling different types of LMOs and what measures are to be put in place when doing so.

E. Regulations, policies and guidelines

20. No guidelines focusing specifically on synthetic biology, either in place or under development, were mentioned in the submissions.

21. However, several submissions noted that their existing biosafety laws for regulating LMOs are also applicable to living organisms that have been developed through synthetic biology. Furthermore, some Parties, one non-Party and several organizations indicated that sectoral regulations and instruments already in place, such as chemical regulations, provide the necessary framework for regulating the non-living products of synthetic biology.

F. Knowledge, experience and perspectives of indigenous peoples and local communities

22. There were no submissions made by representatives of indigenous peoples and local communities in response to the Secretariat's notification. However, some Parties stressed the importance of indigenous peoples and local communities being actively involved in the different deliberations on synthetic biology under the Convention and its Protocols.

23. In their submissions, Parties indicated that their existing biosafety frameworks, which they also apply to organisms developed through synthetic biology, have provisions for public participation, including specific provisions for consulting indigenous peoples and local communities. Such consultations take place through various means, including having a specific liaison to work closely with them where activities may have applications or implications for the natural environment.

24. One Party also noted the importance of including an analysis of the impact of synthetic biology on the economic and social aspects of biodiversity in the mandate of the Ad Hoc Technical Expert Group on Socio-economic Considerations under the Cartagena Protocol.

III. SYNTHESIS OF VIEWS SHARED THROUGH THE ONLINE FORUM

25. The Open-ended Online Forum on Synthetic Biology was convened through the Biosafety-Clearing House⁷ between July and September 2017. A total of 410 interventions were made during that period.

26. The topics of discussion were drawn from the terms of reference of the Ad Hoc Technical Expert Group as follows:

(a) Reviewing recent technological developments within the field of synthetic biology to assess if the developments could lead to impacts on biodiversity and the three objectives of the Convention, including unexpected and significant impacts (moderated by Mr. Casper Linnestad from Norway);

(b) Further analysis of evidence of benefits and adverse effects of organisms, components and products of synthetic biology vis-à-vis the three objectives of the Convention (moderated by Ms. María Andrea Orjuela Restrepo from Mexico);

(c) Identifying any living organisms already developed or currently under research and development through techniques of synthetic biology which do not fall under the definition of living modified organisms under the Cartagena Protocol and evaluating the availability of tools to detect and monitor the organisms, components and products of synthetic biology (moderated by Mr. Nikolai Tsvetkov from Bulgaria);

(d) Gathering information on risk management measures, safe use and best practices for safe handling of organisms, components and products of synthetic biology (moderated by Mr. Benson Kinyagia from Kenya);

27. The present note 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.

⁷ The discussions under the Open-ended Online Forum on Synthetic Biology are available at <http://bch.cbd.int/synbio/open-ended/discussion/>

28. This section provides a compilation of the moderator's summaries of each of the online discussions.

A. Reviewing recent technological developments within the field of synthetic biology to assess if the developments could lead to impacts on biodiversity and the three objectives of the Convention, including unexpected and significant impacts

29. In reviewing the potential impacts, including unexpected and significant adverse effects, of the most recent technological developments in synthetic biology on biodiversity and the three objectives of the Convention the participants of the forum reiterated several of the issues that were brought up in previous discussions.

30. Negative impacts listed by participants included risks arising from horizontal gene transfer leading to alterations in genetic biodiversity and a spread of undesirable phenotypes, effects on non-target organisms, invasiveness resulting from increased fitness.

31. There were also concerns regarding the use of organisms resulting from synthetic biology for the generation of biofuel and bioenergy whereby the increased demand for biomass might lead to the establishment of plantations in former forests, the harvesting of natural grasslands, and pressures on deserts and wetlands. In addition, the increased agricultural activity could result in a decline in soil fertility and structure. Some participants also mentioned that having fewer barriers to "digital biopiracy" might lead to negative impacts on the implementation of access and benefit-sharing arrangements.

32. The use of the CRISPR/Cas9 system was heavily discussed, particularly in the context of mosquito population control, and how such a technology could lead to unexpected outcomes due to off-target effects, such as unexpected and unpredictable changes in the genomes and thus in the phenotype of an organism and its descendants. Participants also elaborated that, while organisms may experience mutations that occur naturally and spontaneously, there are natural mechanisms within the organism that have evolved to provide tight regulatory checks, such as epigenetic regulation, of such mutations. Artificial genetic modification, however, is designed to override such regulation. Therefore, claimed some participants, organisms containing such modifications should be considered experimental and, given the precautionary principal, not considered as ready for commercialization or ecological release.

33. There was also some discussion of biosafety considerations related to organisms resulting from synthetic biology that are currently under development or in use within contained environments that may be accidentally or unintentionally released into the environment. This was of particular concern in the context of organisms containing gene drive systems. This issue was presented in the context of whether or not the research on organisms designed to contain gene drives should be carried out in facilities that are at Biosafety Level 3 or 4 in order to ensure that there is a minimal risk of such organisms being released into the environment.

34. Furthermore, there were some concerns raised regarding the potential legal gaps that may be raised in the context of applying the Nagoya Protocol to the fair and equitable sharing of genetic resources on which synthetic biology applications are reliant.

35. Finally, representatives of indigenous peoples and local communities emphasized that synthetic biology continues to be a controversial issue that is experimental and its consequences on living things, humanity and Mother Earth are still unknown.

36. They also stressed that the modification of living organisms and their subsequent interaction with the environment may lead to ecological changes, in particular the risk of indigenous seed contamination, which may lead to the loss of natural genetic diversity within a short time frame.

37. In expressing their views on the potential benefits of synthetic biology, participants listed a number of applications in which synthetic biology technologies are beneficial, including public health/medicine, agriculture, industrial uses, species conservation, environmental remediation, and invasive species control. They stressed that many of the concerns over potential negative impacts are unfounded as they represent speculative apprehensions that arose with the introduction of LMOs in the past but did not materialize. They also stressed that the techniques that are commonly used under the umbrella term that is “synthetic biology” are simply an extension of methods that are considered modern biotechnology and, as such, they can be dealt with similarly.

38. Participants also indicated that some of the benefits imparted, based on past experience, included a reduction in soil erosion, decreased fuel and chemical pesticide use, increased disease and pest-resistance within plants, increasing on-farm insect biodiversity, raising crop product quality, and improving farm productivity and farmer income. Furthermore, it was noted replacing natural products with synthetic ones could reduce pressure on natural habitats.

39. They also noted that some of the potential negative effects are not unique to synthetic biology but, rather, are issues that are common to the introduction of new technology in general, be it through products derived through synthetic biology, other novel manufacturing processes, or more traditional routes, such as non-biological chemical synthesis and product substitution/replacement.

40. Some participants also pointed out that any perceived gaps in knowledge that might arise from potential adverse effects would only be filled through encouraging research in those areas and that any effort to discourage or suppress such research would only serve to prevent such knowledge from being obtained.

41. Furthermore, in elaborating on the supposed off-target effects that accompany CRISPR/Cas9, other participants indicated that the literature on the topic is inconclusive and that, even in the event that off-target mutations did occur, this would be analogous to mutations that could occur naturally and spontaneously in an organism. Participants also stressed that not all changes in DNA would lead to an effect on the functioning or characteristics of an organism. These participants also claimed that, in the light of the frameworks that are already in place in the context of the Cartagena Protocol, there would probably be no need for new or unique regulations or provisions and that, if new regulations were to be put in place, they would need to be evidence-based and proportionate to risk.

42. In providing an overview on the research and cooperation activities that are being conducted on the possible benefits and potential adverse effects of organisms, components and products of synthetic biology on biodiversity to fill knowledge gaps and identify how those effects relate to the objectives of the Convention and its Protocols, several participants shared a selection research activities that may have a direct link to identifying potential benefits and adverse effects of organisms, components and products of synthetic biology.

(a) A number of new gene editing tools have been developed for research purposes with the view to reducing the off-target effects from CRISPR, such as:

- (i) New CRISPR associated proteins that can operate similar to the Cas9 system including Cpf1 as well as a mini-Cas9 system from *Staphylococcus aureus*;
- (ii) New bacterial genome editing system that combines a yeast-based system with CRISPR-Cas9;
- (iii) *Natronobacterium gregoryi Argonaute* (NgAgo) as a DNA guided endonuclease for gene editing that would be a different approach from CRISPR/TALENs/ZFN etc.;
- (iv) The use of Lambda Red to edit bacterial genomes;

(b) Further to the research and development of gene editing tools, research is also being carried out regarding the possible off-target effects of CRISPR, including the work of Schafer et al,⁸ Wilson et al,⁹ and Chen et al;¹⁰

(c) The [National Institute for Public Health and the Environment \(RIVM\)](#) of the Netherlands commissioned four reports¹¹ which describe experience gained with environmental risk assessment of LMOs and new developments in “white”, “green” and “red” biotechnology.¹² On the basis of these reports, a call for research into the safety aspects of these new developments in modern biotechnology, including synthetic biology, was made in 2016;

(d) RIVM also issued a policy report on gene drives which resulted in the adjustment of Dutch legislation for working with gene drives in contained use facilities.¹³ Furthermore, RIVM is working on aspects of risk assessment for contained use of gene drives in cooperation with several European partners;

(e) RIVM is also conducting research on the potential impact of new technological developments of modern biotechnology on risk assessment methodology. A policy report is expected towards the end of 2017;

(f) The [Commission on Genetic Modification](#), together with the Health Council of the Netherlands, published in 2016 a report that describes major new developments and applications in biotechnology and possible stumbling blocks and (ethical and societal) dilemmas which arise from these developments and trends;¹⁴

(g) Research on Golden Rice demonstrating that, when introgression occurred between the modified plant and the Indian variety Swarna, unexpected gene disruption occurred, which led to extensive disturbance in their growth. The new gene constructs interfered with the non-modified plant's own gene for producing growth hormones, and the additional gene constructs were not, as intended, active solely in the kernels, but also in the leaves;¹⁵

(h) The [German Federal Office of Consumer Protection and Food Safety \(CCBS\)](#) has been monitoring the effects of synthetic biology since 2009. In its first report on monitoring of synthetic biology, which was released in 2012, CCBS concluded that all organisms created with the help of synthetic biology thus far were genetically modified organisms and their risks could be assessed under existing regulations and using existing methodologies. The next report is expected for the end of 2017 and is expected to reach the same conclusions as the 2012 report;

(i) Research being carried out under the ISO/TC 276 biotechnology standards that are being developed by the International Organization for Standardization (ISO);¹⁶

(j) The Defence Advanced Research Projects Agency (DARPA) in the United States of America has developed five programmes that demonstrate the growing complexity of synthetic biology under development that could have a direct impact on the objectives of the Convention. These are:

⁸ <https://www.nature.com/nmeth/journal/v14/n6/full/nmeth.4293.html>

⁹ <http://www.biorxiv.org/content/biorxiv/early/2017/06/21/153338.full.pdf>

¹⁰ <http://www.biorxiv.org/content/early/2017/07/06/160036>

¹¹ These can be found at: <http://www.stw.nl/nl/content/biotechnology-and-safety>

¹² White: Industrial Biotechnology; Green: Plant Biotechnology; Red: Medical Biotechnology

¹³ http://www.rivm.nl/Documenten_en_publicaties/Wetenschappelijk/Rapporten/2016/februari/Gene_drives_Policy_report

¹⁴ This trend analysis can be found at <http://www.cogem.net/index.cfm/en/publications/publication/trend-analysis-biotechnology-2016>.

¹⁵ <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0169600>

¹⁶ Available at <https://www.iso.org/committee/4514241/x/catalogue/p/0/u/1/w/0/d/0>

“Living foundries”, “Biological robustness in complex settings”, “Safe genes”, “Insect allies” and “Ecological niche-preference engineering”;¹⁷

(k) A small pilot project was started by GenØk on plasticity of plant cells that have been genome-edited, and how they can cope with such interventions, focusing on CRISPR off-target activity.¹⁸

43. Several participants indicated that no other recent technological developments had taken place within the field of synthetic biology that needed to be considered. On the other hand, other participants disagreed and pointed to the need for further research in the field of synthetic biology in order to determine whether there are any recent issues that warrant caution.

44. Below is a selection of specific technological developments that have taken place within the field of synthetic biology that were mentioned during the discussion:

(a) The applications of recent synthetic biology techniques expand the possible range of host organisms to all living beings, which is far beyond the range of organisms that were successfully modified through the more traditional modern biotechnology tools;

(b) Many applications of synthetic biology, including those using modified microorganisms, will no longer be under contained use as they are intended to be introduced into the environment;

(c) The application of “big data”, machine learning, artificial intelligence and robotics with a view to constructing genomes, which are expected to enable rapid and automatic prototyping of highly novel organisms;

(d) The development and application of external genome regulation methods, such as RNA interference in the form of sprays to control pests or influence plant characteristics;

(e) The application of CRISPR/Cas-based gene drives in organisms, especially in insects, and the need to thoroughly consider the potential benefits and risks at the ecosystem level;

(f) The increased accessibility of the biotech tools, such as CRISPR kits, to the DIY community and the public at large outside of formal laboratory facilities;

(g) The use of modified algae production for the production of chemical substances poses a need for relatively “open” production ponds/facilities, due to the need for sunlight, which requires well designed either physical or biological safety and containment measures;

(h) Whole cell sensor development is being more actively pursued and, given that such sensors may be used either inside or outside laboratory facilities, it would therefore require well-designed containment strategies;

(i) The development of cell-free systems would require the development of new and appropriate risk assessment methodologies;

(j) Addressing the ever increasing speed of development within the field of biotechnology given that new biotechnology tools combined with automated laboratories, DNA-circuitry design tools and bioinformatics may lead to the production of more modified organisms more rapidly than their risk can be assessed;

¹⁷ Additional information about these programmes can be found at <http://www.darpa.mil/about-us/about-darpa>.

¹⁸ Available at <http://genok.no/the-synplast-project/>

(k) The emerging field of “molecular communication”, which is the application of information theory to molecular processes whereby communication signals, such as those used between organisms, are physically encoded in molecules;

(l) The development of tools to enable the simultaneous targeting of multiple sites, or multiplexing, within a genome at once, often with just one construct/vector using nucleases, such as CRISPR/Cas9 or PTG/Cas9.

B. Further analysing evidence of benefits and adverse effects of organisms, components and products of synthetic biology vis-à-vis the three objectives of the Convention

45. With regard to the benefits and adverse effects of organisms produced through synthetic biology, participants pointed to several of the effects that were brought up during the discussions of the Online Forum and in past meetings on synthetic biology held by the Secretariat of the Convention on Biological Diversity, as outlined in paragraphs 30 to 41 above. A number of references supporting the claims of either benefits or adverse effects of such organisms were included. These references are listed in annex III to document CBD/SYNBIO/AHTEG/2017/1/INF/1.

46. Several participants emphasized that, to date, no organisms that have been developed through synthetic biology techniques have been released into the environment and that any claims of evidence put forward regarding their benefits and adverse effects would therefore be based on models or experiments under contained use, such as in laboratories, and may not be fully reliable. By extension, other participants pointed to the experience gained through the use of “traditional” LMOs which have been released into the environment as an example from which information can be extrapolated regarding the potential benefits and adverse effects of living organisms that have been produced through synthetic biology.

47. Furthermore, some participants noted that the examples provided during the discussion came from research which may not have been carried out to evaluate the impact of the organisms, components or products of synthetic biology on the three objectives of the Convention, particularly since potential benefits and adverse effects on biodiversity are often indirect and difficult to measure.

48. Some participants expressed concern regarding the time frames during which some of the research that was presented as evidence had taken place. They indicated that several of the examples provided stemmed from short-term experiments and analyses that did not cover a large enough amount of time to confirm the benefits and adverse effects on biodiversity of the living organisms produced through synthetic biology. These participants argued that long-term tests are necessary.

49. There was not a significant amount of discussion on the benefits and adverse effects of the components and products of synthetic biology. Several participants agreed that the benefits and adverse effects of components and products of synthetic biology would be similar to those obtained through other techniques. Participants also pointed to the existence of regulations which, although outside the scope of the Convention — including those that focus on pharmaceuticals, chemicals, and food and feed safety — are useful in assessing the benefits and adverse effects of the components and products of synthetic biology. Other participants stated, however, that those regulations were not adequate or sufficient to assess the benefits and adverse effects of all components and products of synthetic biology.

50. Furthermore, some participants highlighted the need to take into account the fair and equitable sharing of the benefits arising out of the utilization of the genetic resources that are used as components of synthetic biology applications, including in the context of digital sequence information.

51. In addition to the comments made regarding the topic of discussion, there were also several interventions on the issue of risk assessment. Several participants reiterated that current risk assessment methodologies are being applied to organisms produced by synthetic biology. On the other hand, other participants indicated that current risk assessment methodologies, which are based on the principles outlined in Annex III of the Cartagena Protocol, may not be adequate to assess the risks of organisms that were developed through techniques that did not exist when the Cartagena Protocol was negotiated. Such techniques include gene drive technologies and LMOs for which there may not be an appropriate comparator. Therefore, these participants noted that assessing the risk of these LMOs may not be possible under existing frameworks that use the methodology in Annex III as the basis for their risk assessments. In the light of this, some participants suggested that the experience gained from invasive alien species, such as the unintended negative impacts of biocontrol agents, could provide useful information on potential adverse effects that may need to be considered when assessing the risks of organisms developed through synthetic biology that may be released into the environment.

52. Finally, notwithstanding the scope and objective of the Cartagena Protocol on Biosafety, some participants noted that the phenotype of an organism, rather than the method by which it was produced, should dictate the need to assess the risks and potential impacts on biodiversity. They also pointed to research that is taking place in order to limit the possible adverse effects of gene drives, such as self-limiting gene-drive technologies, taking into account among other things the likelihood for the development of resistance to gene drive systems.

C. Identifying any living organism already developed or currently under research and development through techniques of synthetic biology that do not fall under the definition of living modified organisms contained in the Cartagena Protocol

53. Participants generally agreed that most, if not all, living organisms that are already developed or are currently under research and development through techniques of synthetic biology fall under the definition of living modified organisms under the Cartagena Protocol. Several participants also pointed to the link this has to the application of relevant risk assessment methodologies as per Annex III.

54. Participants provided the following examples of organisms developed through synthetic biology techniques that are LMOs:

(a) The *Mycoplasma mycoides* bacterium, developed by the J. Craig Venter Institute, which is a bacterial cell into which a synthetic genome that is different from the genome of the recipient cell has been inserted. The resulting organism was found to have all the characteristics defined by the synthesized genome;

(b) A Baker's yeast or *Saccharomyces cerevisiae*, Sc2.0, which is being modified to redesign all 16 chromosomes in such a way that they are computationally designed and assembled using DNA synthesis and molecular biology techniques;

(c) Semi-synthetic (xenobiology) organisms containing an expanded genetic alphabet developed through the use of unnatural base pairs. Such organisms, at present, are based on manipulating nucleic acids.

55. There was some disagreement over the classification of organisms resulting from gene editing techniques and cisgenesis.¹⁹ Some participants were of the view that such organisms fit the definition of LMOs since they are derived through the application of modern biotechnology to produce a living

¹⁹ Cisgenesis is the genetic modification of a recipient organism with a natural gene from a crossable — sexually compatible — organism. Adapted from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1525145/>

organism that has a novel combination of genetic material. On the other hand, some participants were of the view that organisms developed through gene editing or total genome synthesis may contain only single or few base-pair changes which could have been obtained through traditional breeding techniques (including natural and induced mutations); in such cases, these organisms would not be LMOs.

56. Likewise, some participants also argued that organisms developed through cisgenesis do not “overcome natural physiological reproductive or recombination barriers” as the modified genetic material originates from the recipient organism itself; following the same logic, an organism developed through cisgenesis would be an LMO if it contained any novel combination of genetic material that could not be obtained through natural recombination or traditional breeding (for example, a piece of foreign DNA, such as a transcription terminator or vector backbone).

57. Several participants also highlighted some examples of grey areas of synthetic biology research where the resulting outcome may need to be monitored as they are developed due to their potential impact on biological diversity and, in some cases to determine whether or not they fit the definition of an LMO as per the Cartagena Protocol once they are developed. Such examples included:

(a) The development of artificial self-replicating cells, or protocells. While there is research being conducted in this area, there are currently no examples of self-replicating protocells. In addition, most of the research groups working in this area are exploring protocells based on nucleic acids, which, if successful, may therefore also be considered an LMO under the Cartagena Protocol;

(b) The development of cell-free systems for protein synthesis. Such systems may have implications at two levels; the first is the possibility that from such a system viable organisms may emerge, e.g. when used to pack genetic elements into viral particles. Secondly, such cell-free systems may use genetic resources and “bioparts” and potentially be scaled up to produce compounds that could replace naturally sourced products, thereby impacting sustainable use and equitable sharing of benefits from biodiversity;

(c) Use of manipulations that do not lead to a “novel combination of genetic material”, such as the injection or spraying of functional RNA/DNA molecules for vaccination, immunotherapy or agricultural pathogen control;

(d) Use of techniques that do not involve “in vitro nucleic acid techniques”, such as supplementation-based incorporation of non-canonical amino acids at the protein level whereby, for example, a microorganism is starved of a specific natural amino acid, forcing the organism to incorporate a structurally similar synthetic amino acid into its proteins instead;

(e) Organisms that have been modified through epigenetic engineering, such as histone modification and DNA methylation, for the purpose of altering gene expression. Such organisms may have altered biological properties without having “a novel combination of genetic material” if the term “genetic material” is strictly understood to refer to changes in the sequence of nucleic acids.

58. In an attempt to facilitate the discussions of the Ad Hoc Technical Expert Group, a table comparing the different types of organisms and techniques mentioned against each of the criteria in the definition of an LMO has been developed (see table below).

Table. **Comparison of the different types of organisms and techniques mentioned against each of the criteria in the definition of a living modified organism**

	Living organism	Living modified organism	Obtained through modern biotechnology	
	Capable of transferring or replicating genetic material	Possesses a novel combination of genetic material	In vitro nucleic acid techniques	Overcome natural physiological reproductive or recombination barriers and are not techniques used in traditional breeding and selection
Total <i>in vitro</i> synthesis of genomes or individual chromosomes, e.g. <i>Mycoplasma mycoides</i> , <i>Mycoplasma</i> derived minimal cell and Sc2.0	✓	✓	✓	✓ (most cases) ? ²⁰
Genome editing techniques	✓	✓	✓	✓ (most cases) ? ²¹
Cisgenesis	✓	✓	✓	✓ (most cases) ? ²²
Xenobiology, e.g. organisms contacting non-natural nucleotides and amino acids	✓	✓	✓	✓ x ²³
<i>De novo</i> engineered proteins, RNAs, signalling and metabolic pathways, incl. such without analogs in nature	✓	✓	✓	✓
RNA/DNA-based manipulations	✓	? ²⁴	✓	?

²⁰ In theory, when only minimal changes are introduced, similar changes could result from recombination thereby not fulfilling the definition of modern biotechnology.

²¹ In theory, when only minimal changes are introduced, similar changes could result from recombination thereby not fulfilling the definition of modern biotechnology.

²² In theory, when only genetic material from a species that is sexually compatible with the recipient organism is introduced, similar changes could be obtained through traditional breeding and selection.

²³ When auxotrophic mutants are fed with non-natural nucleotides or amino acids.

²⁴ Those nucleic acids are only transiently present in the cell, but during that time there can be expression of genetic information.

	Living organism	Living modified organism	Obtained through modern biotechnology	
Epigenetic engineering	✓	γ ²⁵	✓	γ ²⁶
			× ²⁷	
Protocells	γ ²⁸	✓	✓	✓
Cell-free systems	×	✓ ²⁹	✓	✓

Note: The table above was prepared on the assumption that “natural physiological reproductive or recombination barriers” envisioned are not absolute. Horizontal gene transfer can occur in principle between any two organisms and genes with any sequence can evolve if necessary and if unlimited time is available. In this sense, modern biotechnology overcomes barriers not so much by making impossible things possible, but, rather, by allowing for things that would take an unrealistic amount of time to be done if other methods were used.

D. Evaluating the availability of tools to detect and monitor the organisms, components and products of synthetic biology

59. With regard to evaluating the availability of tools to detect and monitor the organisms, components and products of synthetic biology, some participants pointed to some common methods that may be useful in detecting and monitoring organisms of synthetic biology that target the modified DNA sequences through PCR-based amplification.

60. Several participants also pointed to the difficulties that may arise with LMOs that may have been produced through gene editing, cisgenesis or genome synthesis and, as such, may not have a suitable target marker due to the changes being indistinguishable from naturally occurring counterparts. Suggestions for the inclusion of a suitable marker gene or “watermark” were made by some participants.

61. With regard to detecting products of synthetic biology, it was highlighted that this may also be possible through the application of analytical chemistry techniques that may be able to distinguish between products of synthetic biology and naturally occurring or chemically synthesized counterparts by detecting for the presence of other substances that will vary depending on the source.

62. On the other hand, several participants were of the opinion that no statements can be made about monitoring tools at this stage because the need for such tools would be dependent on the properties of the organism in question. Any monitoring measures would be put in place as part of a risk analysis performed on a case-by-case basis as an outcome of assessing the risk of a particular organism. These participants were of the view that the need for monitoring tools cannot be discussed in a generic manner.

²⁵ It is unclear whether “novel combination of genetic material” refers only to the nucleic acid sequence or if it includes the proteins involved in packing the chromatin that lead to epigenetic modifications, which in some cases may be inherited for some generations.

²⁶ It is unclear whether epigenetic changes can be considered overcoming natural reproductive or recombination barrier.

²⁷ Only in some cases. Epigenetic changes can be introduced through pharmacological agents as well.

²⁸ No protocell capable of transferring genetic material exists at present; replication can happen in some model systems, but it is more like a cell-free system.

²⁹ Usually in such cell-free systems, recombinant nucleic acid molecules are used, e.g. systems for cell-free expression of proteins.

E. Gathering information on risk management measures, safe use and best practices for safe handling of organisms, components and products of synthetic biology

63. In general, participants emphasized the importance of having robust risk management practices in place in order to ensure that the three objectives of the convention are met and that provisions are in place for the safe handling of organisms, protecting safety, health, and the environment. At the same time, other participants highlighted the need for dealing with synthetic biology in a way that allows for innovation and societal benefit from its potential contributions to global biodiversity, without imposing lengthy and costly regulatory processes.

64. Participants generally agreed that current risk management measures and best practices, such as confinement strategies, restrictions on use, monitoring and reporting requirements, and contingency plans, that are in use for “traditional” LMOs are also sufficient in the context of living organisms developed through current and near future applications of synthetic biology. Nonetheless, some participants also emphasized that, while such measures may be adequate for the time being, more research and evaluation might be needed as advances in the field of synthetic biology continue. Moreover, some participants noted that recommendations and decisions regarding the need for risk management measures are made on a case-by-case basis depending on the organism and type of risk being managed and, for this reason, general discussions on risk management strategies for synthetic biology applications are of limited value.

65. With respect to the components (e.g. a DNA molecule) and products (e.g. a chemical substance produced by an organism) of synthetic biology, in discussing the extent to which current risk management measures and best practices are sufficient, several participants pointed to the existence of national and international legislation governing the handling and risk management of chemical substances whether they were produced using chemical synthesis or synthetic biology. Such legislation includes laws that focus on industrial chemicals, plant protection products, food additives, medicinal products and biological weaponry, among others. On the other hand, some participants emphasized that such provisions would only cover those products that are captured by specific product-related legislation and may focus more on the trade-related matters as opposed to their impact on the three objectives of the Convention. Therefore, some risk management measures relating to components and products of synthetic biology may be overlooked.

66. With regard to participants foreseeing a need for adapting safety measures in the future as developments in the field of synthetic biology are made, participants indicated that the approaches that currently in place are inherently adaptable and flexible enough to accommodate new knowledge due to the case-by-case nature of risk management practices. However, concerns were raised regarding the capacity of regulatory agencies to stay abreast of the increased influx of cases involving new organisms and their ability to efficiently provide the quantity and quality of new risk management measures that will be required.

67. There were no concrete examples of existing applications of synthetic biology for which risk management measures may not be sufficient to ensure the safe handling and use of living organisms developed through synthetic biology. However, several participants raised concern about organisms produced through synthetic biology that are designed to interact with and modify existing ecosystems, specifically those containing gene drives. Some participants indicated that this is an area where additional guidance in the context of the objectives of the Convention and its Protocols is needed.

68. Some participants were of the view that specific new areas of research aimed at ensuring the safe use of current and near future applications of synthetic biology were not needed. These participants also emphasized that, due to the varied nature of organisms produced through synthetic biology techniques,

ranging from microorganisms to plants to insects, it may be more useful to consider the risk management of such organisms in a more specific context based on their intended use rather than under the umbrella of synthetic biology, which is too broad a categorization and may not serve to fill the necessary knowledge gaps relating to their safety. Other participants provided specific examples of areas where more research may be needed, including the interface of synthetic biology and ecology specifically focusing on gene transfer, direct competition, and habitat modification resulting from the interaction between organisms produced through synthetic biology and other species.

69. Finally, several participants submitted references, as outlined in CBD/SYNBIO/AHTEG/2017/1/INF/1, annex III, relating to guidelines and guidance on risk management measures that may be applicable to organisms, components and products of synthetic biology.

IV. OTHER RELEVANT PROCESSES UNDER THE CONVENTION AND ITS PROTOCOLS

70. In considering its recommendations to the Subsidiary Body on Scientific, Technical and Technological Advice at its twenty-second meeting, the Ad Hoc Technical Expert Group may wish to consider other processes that are taking place under the Convention and its Protocols in order to facilitate the execution of future activities related to synthetic biology in a coordinated manner.

A. Processes for the identification of new and emerging issues

71. During the intersessional period, a recommendation was proposed to review the process for the identification of new and emerging issues. Parties and relevant organizations were therefore invited³⁰ to submit views on the process for the identification of new and emerging issues, including how to apply the criteria set out in paragraph 12 of decision IX/29.

72. On the basis of the information received, the Executive Secretary issued a note for consideration by the Subsidiary Body on Scientific, Technical and Technological Advice at its twenty-first meeting ([CBD/SBSTTA/21/8](#)). The note includes a summary of the views submitted by Parties and relevant organizations on the process for identifying new and emerging issues as well as a suggested recommendation on a way forward.

73. Recalling that the Ad Hoc Technical Expert Group was mandated to provide an analysis against the criteria set out in paragraph 12 of decision IX/29 for the identification of new and emerging issues to contribute to the completion of the assessment requested in paragraph 2 of decision XII/24, and taking into account the ongoing deliberations by the Subsidiary Body on Scientific, Technical and Technological Advice, the Group may wish to consider deferring further analyses of synthetic biology against the criteria set out in paragraph 12 of decision IX/29 until further guidance on how to apply the said criteria is provided by the Conference of the Parties.

B. Knowledge, experience and perspectives of indigenous peoples and local communities

74. In its decision XIII/17, the Conference of the Parties invited Parties, other Governments, relevant organizations and indigenous peoples and local communities to submit to the Executive Secretary information and supporting documentation on, inter alia, knowledge, experience and perspectives of indigenous peoples and local communities in the context of living in harmony with nature for comparison and better understanding of the potential benefits and adverse effects of synthetic biology.

³⁰ Notification SCBD/OES/DC/RH/84326, available at <https://www.cbd.int/doc/notifications/2017/ntf-2017-054-newemergingissues-en.pdf>.

75. “Living in harmony with nature” is the theme of the 2050 Vision of the Strategic Plan for Biodiversity 2011-2020, which was adopted at the tenth meeting of the Conference of the Parties. Its vision statement is: “Living in harmony with nature”, where “By 2050, biodiversity is valued, conserved, restored and wisely used, maintaining ecosystem services, sustaining a healthy planet and delivering benefits essential for all people.”³¹

76. The notion of living in harmony with nature considers different visions, approaches and tools for the conservation and sustainable use of biodiversity and invites the mainstreaming of the concept of living in harmony with nature across the various sectors.

77. In the light of this and taking into account the multi-year programme of work of the Conference of the Parties up to 2020,³² the Conference of the Parties, in its decision XII/2 C, paragraph 4, invited the Executive Secretary, subject to availability of resources, to facilitate the organization of an interactive dialogue on living in harmony with nature at the thirteenth meeting of the Conference of the Parties, and invited the United Nations General Assembly to make available to the Conference of the Parties at its thirteenth meeting the outcomes of the interactive dialogues on harmony with nature of the United Nations General Assembly.³³

78. To facilitate the deliberations of the Ad Hoc Technical Expert Group on this topic, the outcomes of the interactive dialogue on the theme “Living in harmony with nature”, which took place during the thirteenth meeting of the Conference of the Parties, is being made available as CBD/SYNBIO/AHTEG/2017/1/INF/2.³⁴

C. Risk assessment and risk management under the Cartagena Protocol

79. In its decision BS-VIII/12, the Conference of the Parties serving as the meeting of the Parties to the Cartagena Protocol invited Parties to submit to the Executive Secretary:

- (a) Information on their needs and priorities for further guidance on specific topics of risk assessment of living modified organisms;
- (b) Proposals on criteria, including the technical justification, that may facilitate the selection of topics for the development of further guidance;
- (c) Views on perceived gaps in existing guidance materials.

80. The Parties also 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.

81. The Subsidiary Body on Scientific, Technical and Technological Advice was requested to review the information provided and to recommend a way forward to address the needs, priorities and gaps identified by Parties for consideration by the Conference of the Parties serving as the meeting of the Parties to the Cartagena Protocol at its ninth meeting, including the possible establishment of a new ad hoc technical expert group.

³¹ [Decision X/2](#), annex.

³² [Decision XII/31](#).

³³ <http://harmonywithnatureun.org/index.html>

³⁴ The outcomes of the interactive dialogue were originally issued as annex III of the report of the Conference of the Parties on its thirteenth meeting ([CBD/COP/13/25](#)).

82. In response, 19 Parties have provided the information referred to in paragraph 79 above. The majority of Parties (12) identified at least one topic among their needs and priorities for the development of further guidance on risk assessment of LMOs. Among these, 10 Parties prioritized the development of guidance on risk assessment of organisms developed through synthetic biology, and in particular of organisms produced through genome editing or RNAi techniques, and of organisms carrying gene drives.

83. Among the criteria to select topics for the development of further guidance, several Parties indicated that new guidance should focus on:

- (a) Specific topics with potential adverse effects on biodiversity and/or human health;
- (b) Risk assessment regarding organisms or characteristics that cannot be performed by using existing guidance documents;
- (c) Organisms that have already been or are likely to be released into the environment and/or commercialized;
- (d) Specific topics with a high pace of scientific and technological advancement.

D. Socio-economic considerations under the Cartagena Protocol

84. At its sixth meeting³⁵ the Conference of the Parties serving as the meeting of the Parties to the Cartagena Protocol decided to establish an Ad Hoc Technical Expert Group on Socio-economic Considerations with a view to developing conceptual clarity in the context of Article 26, paragraph 1, of the Protocol, which provides that, in reaching a decision on import under this Protocol or under its domestic measures implementing the Protocol, Parties may take into account, consistent with their international obligations, socio-economic considerations arising from the impact of living modified organisms on the conservation and sustainable use of biological diversity, especially with regard to the value of biological diversity to indigenous and local communities.

85. The outcome of the work of the Ad Hoc Technical Expert Group on Socio-economic Considerations thus far has been the development of the “Draft guidance on the assessment of socio-economic considerations in the context of Article 26 of the Cartagena Protocol on Biosafety”.³⁶

86. The draft guidance provides, among other things, principles for the assessment of socio-economic considerations and outlines the stages of such an assessment process. The guidance also refers, among other things, to different cultural practices, religious beliefs and practices, and indigenous, traditional and local knowledge and practices as well as the value of biodiversity to indigenous people and local communities.

E. Detection and identification of living modified organisms under the Cartagena Protocol

87. At its fifth meeting,³⁷ the Conference of the Parties serving as the meeting of the Parties to the Cartagena Protocol mandated a number of activities for laboratories involved in the detection and identification of living modified organisms. Specifically, the Parties requested the establishment, through the Biosafety Clearing-House, of an electronic network of laboratories involved in the detection and identification of LMOs and the organization of workshops for heads of detection laboratories.

³⁵ See [decision BS-VI/13](#).

³⁶ Available at <https://www.cbd.int/meetings/CPSEC-AHTEG-2017-01>

³⁷ See [decision BS-V/9](#).

88. Since the establishment of the Network several online and face-to-face activities focusing on the sampling, detection and identification of LMOs have taken place with a view to assisting Parties in fulfilling the requirements under the relevant articles of the Cartagena Protocol and towards achieving the relevant outcomes of the Strategic Plan for implementation of the Cartagena Protocol.

89. Among the outcomes of their work are the development of technical tools and of a draft training manual for capacity-building activities on the detection and identification on LMOs. To date, the text of the draft training manual has been finalized, and the manual is currently under review by the members of the Network.

F. Potential implications of the use of digital sequence information on genetic resources for the objectives of the Convention on Biological Diversity and the Nagoya Protocol

90. In the light of the discussions on digital sequence information on genetic resources that were initiated by the Online Forum and Ad Hoc Technical Expert Group on Synthetic Biology during the 2014-2016 intersessional period, the Conference of the Parties took up the issue and adopted [decision XIII/16](#),³⁸ in which it decided to consider, at its fourteenth meeting, any potential implications of the use of digital sequence information on genetic resources for the objectives of the Convention on Biological Diversity.

91. In the decision, Parties, other Governments, indigenous peoples and local communities as well as relevant organizations and stakeholders were invited to submit views and relevant information to the Executive Secretary on any such potential implications.

92. Furthermore, in the same decision, the Parties requested that the Executive Secretary commission a fact-finding and scoping study to clarify terminology and concepts and to assess the extent and the terms and conditions of the use of digital sequence information on genetic resources in the context of the Convention and the Nagoya Protocol.

93. Finally, the decision established an ad hoc technical expert group focusing on digital sequence information on genetic resources, which was mandated to:

(a) Consider the compilation, synthesis and the study referred to above in order to examine any potential implications of the use of digital sequence information on genetic resources for the three objectives of the Convention and the objective of the Nagoya Protocol and implementation to achieve these objectives;

(b) Consider the technical scope and legal and scientific implications of existing terminology related to digital sequence information on genetic resources;

(c) Identify the different types of digital sequence information on genetic resources that are relevant to the Convention and the Nagoya Protocol.

94. As of the time of writing, several activities have taken place with a view to complying with the various elements of this decision. The submission of views pursuant to paragraph 91 has been completed,³⁹ and the selection of the members of the Ad Hoc Technical Expert Group on Digital

³⁸ This decision was mirrored by the Conference of the Parties serving as the meeting of the Parties to the Nagoya Protocol, which adopted [decision NP-2/14](#), wherein it also decided to consider, at its third meeting, any potential implications of the use of digital sequence information on genetic resources for the objective of the Nagoya Protocol.

³⁹ Submissions are available at <https://www.cbd.int/abs/dsi-gr/ahteg.shtml#submissions>

Sequence Information on Genetic Resources has been finalized.⁴⁰ Furthermore, the fact-finding and scoping study has been commissioned and is being made available for peer review.⁴¹ The study will be finalized, taking into account the comments from the peer review, prior to the meeting of the Ad Hoc Technical Expert Group on Digital Sequence Information on Genetic Resources.

95. The Ad Hoc Technical Expert Group on Digital Sequence Information on Genetic Resources will submit its outcomes for consideration by the Subsidiary Body on Scientific, Technical and Technological Advice at its twenty-second meeting, which will consider the outcomes and make a recommendation on the potential implications of the use of digital sequence information on genetic resources for the three objectives of the Convention for the consideration of the Conference of the Parties at its fourteenth meeting.

V. CONCLUSIONS

96. From the submissions and views shared through the Online Forum, it is evident that synthetic biology continues to play an important role in applications that are related to and may have an impact on the three objectives of the Conventions and its Protocols.

97. Among the potential benefits arising from synthetic biology applications is the development of efficient and effective ways to respond to challenges associated with bioenergy, agriculture, health and chemical production, among other applications. On the other hand, there are several examples of potential adverse effects that may arise from the use of synthetic biology through invasiveness, persistence, and unintended and irreversible consequences resulting from the altering of natural populations due to intentional or unintentional introduction into the environment as well as the extension of the adverse effects into other countries due to possible transboundary movements. There is currently research taking place with a view to reducing the off-target effects from gene editing tools. There is also work being carried out to develop policy that focuses on the use of gene drives in contained use facilities with a view to working on aspects of soundly assessing the risks that may arise from organisms containing gene drives.

98. Organisms that are of particular concern include those that are developed using genome editing tools, those containing gene drives, and, in particular, those that are intended for release into the environment. While the potential benefits of organisms produced through the use of such tools are numerous, ranging from the control of mosquito populations and vector-borne diseases to eradication of invasive alien species, there continue to be significant concerns regarding the potential adverse effects at the ecosystem level arising from techniques aimed at irreversibly altering natural populations, as well as from off-target and other unintended effects.

99. With regard to the assessment of potential benefits and adverse effects of organisms that have been developed through synthetic biology techniques and that may be intended for release into the environment, it was noted that, to date, any claims of evidence put forward regarding their benefits and adverse effects would be based on models or on experiments under contained use. Such experiments would have taken place over short spans of time and may not have been specifically focused on assessing the impact of the organisms, components and products of synthetic biology on the three objectives of the Convention.

100. Limited knowledge and a high level of uncertainty are of particular concern in the context of risk assessment of organisms containing gene drive systems.

⁴⁰ Notification SCBD/SPS/DC/VN/KG/NH/86630, available at <https://www.cbd.int/abs/dsi-gr/ahteg.shtml#submissions>.

⁴¹ Information regarding the peer review is available at <https://www.cbd.int/abs/dsi-gr/ahteg.shtml#peerreview>.

101. In contrast, calls are made to draw from the experience gained through the use of “traditional” LMOs which have been released into the environment as an example from which information can be extrapolated regarding the potential benefits and adverse effects of living organisms that are produced through synthetic biology and that may be released into the environment in the future.

102. There continues to be a general view that most, if not all, living organisms that have already been developed, or are currently under research and development, through techniques of synthetic biology fall under the definition of living modified organisms as per the Cartagena Protocol. However, there is some debate as to whether all genome editing, cisgenesis and epigenetic engineering techniques would “overcome natural physiological reproductive or recombination barriers”, in which case some of the resulting LMOs could fall outside the definition of LMOs under the Cartagena Protocol. It remains unclear if artificial self-replicating cells or protocells are to be considered as “living” or not.

103. With respect to the risk assessment and risk management of organisms resulting from synthetic biology, the submissions and discussions placed emphasis on the importance of having robust risk assessment and risk management practices in place, while also ensuring that innovation and the societal benefits of synthetic biology are not hampered. It is noted that some countries with robust biosafety regulations have put in place risk assessment methodologies and risk management measures for “traditional” LMOs, and it is suggested that these are flexible enough to accommodate new knowledge due to the case-by-case nature of risk assessment and risk management processes. It is also noted that, as organisms become more complex with advances in synthetic biology, adaptations are being made to existing risk assessment and risk management methodologies in order to address the challenges that come with such organisms, for example the absence of suitable comparators, and the presence of multiple modifications which may interact in unknown ways, resulting in unexpected outcomes. There is also particular concern regarding organisms containing gene drive systems that are intended for release into the environment or that may be accidentally or unintentionally released into the environment.

104. With regard to the risk assessment of components and products of synthetic biology, references have been made to other more relevant legislation under which these are regulated; however, there are concerns that such regulations are not adequate to address all potential impacts on the three objectives of the Convention.

105. Tools to detect and monitor organisms and components of synthetic biology are available and primarily target modified DNA sequences through PCR-based amplification, while products of synthetic biology can be detected using analytical chemistry techniques. However, there continue to be challenges in detecting organisms resulting from synthetic biology for which there might not be a suitable target marker or those that are indistinguishable from organisms developed through methods other than modern biotechnology, such as induced mutation, or from naturally occurring counterparts.

106. There continue to be knowledge gaps, uncertainty and some concern among members of indigenous peoples and local communities regarding the possible impact of synthetic biology on their livelihoods, ethical, social and religious values, and their ability to live in harmony with nature.
