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NEW AND EMERGING ISSUES: SYNTHETIC BIOLOGY

Note by the Executive Secretary

I. INTRODUCTION

1. In decision XI/11 on new and emerging issues relating to the conservation and sustainable use of biodiversity the Conference of the Parties took note of the proposals for new and emerging issues relating to the conservation and sustainable use of biodiversity.

2. Recognizing the development of technologies associated with synthetic life, cells or genomes, and the scientific uncertainties of their potential impact on the conservation and sustainable use of biological diversity, the Conference of the Parties urged Parties and invited other Governments to take a precautionary approach, in accordance with the preamble of the Convention and with Article 14, when addressing threats of significant reduction or loss of biological diversity posed by organisms, components and products resulting from synthetic biology, in accordance with domestic legislation and other relevant international obligations.

3. The Conference of the Parties also requested the Executive Secretary to:

(a) Invite Parties, other Governments, relevant international organizations, indigenous and local communities and other stakeholders to submit, in accordance with paragraphs 11 and 12 of decision IX/29, additional relevant information on components, organisms and products resulting from synthetic biology techniques that may have impacts on the conservation and sustainable use of biological diversity and associated social, economic and cultural considerations;

(b) Compile and synthesize relevant available information, together with the accompanying information;

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(c) Consider possible gaps and overlaps with the applicable provisions of the Convention, its Protocols and other relevant agreements related to components, organisms and products resulting from synthetic biology techniques;

(d) Make a synthesis of the above information, including an analysis of how the criteria set out in paragraph 12 of decision IX/29 apply to this issue, available for peer-review and subsequent consideration by a meeting of the Subsidiary Body on Scientific, Technical and Technological Advice prior to the twelfth meeting of the Conference of the Parties, in accordance with paragraph 13 of decision IX/29.

4. In response to this decision, the Executive Secretary issued notification 2013-018 (Ref. No. SCBD/STTM/DC/RH/VA/81439), dated 22 February 2013, inviting additional information on synthetic biology and undertook a review of information in accordance with paragraph 5 of decision XI/11. The Executive Secretary made available for peer-review draft documents on potential positive and negative impacts of synthetic biology and on gaps and overlaps with the Convention, its Protocols and other relevant agreements and made the peer-review comments available online. The Executive Secretary, with the financial support from the United Kingdom of Great Britain and Northern Ireland, revised and completed these documents in light of the comments received. The completed documents are made available for the information of the Subsidiary Body as information documents UNEP/CBD/SBSTTA/18/INF/3 and INF/4.

5. This note is intended to assist the Subsidiary Body on Scientific, Technical and Technological Advice in assessing how the criteria set out in paragraph 12 of decision IX/29 apply to synthetic biology and in preparing a recommendation to the Conference of the Parties on this issue.

6. The document provides an overview of synthetic biology; discusses its potential positive and negative impacts on the conservation and sustainable use of biological diversity; and considers possible gaps and overlaps with the applicable provisions of the Convention, its Protocols and other relevant agreements (section II). In section III, the criteria for identifying new and emerging issues related to the conservation and sustainable use of biodiversity are applied. Section IV contains draft recommendations.

II. OVERVIEW OF SYNTHETIC BIOLOGY, ITS POTENTIAL POSITIVE AND NEGATIVE IMPACTS, AND POSSIBLE GAPS AND OVERLAPS WITH THE CONVENTION, ITS PROTOCOLS AND INTERNATIONAL LAW

A. Areas of research and applications commonly considered to be synthetic biology

7. **One of the most commonly cited definitions of synthetic biology is "the design and construction of new biological parts, devices, and systems" and "the re-design of existing, natural biological systems for useful purposes."** Although there is no legally accepted definition, there is general agreement that synthetic biology aims to *exercise control* in the design, characterization and construction of biological parts, devices and systems, leading to *more predictable* designed biological systems. Key features of synthetic biology include chemical synthesis of genetic sequences and an engineering-based approach. Synthetic biology represents a shift in the driving forces of biology, from discovery and observation to hypothesis and synthesis. Sometimes described as a "converging technology," synthetic biology brings together and builds on the fields of engineering, molecular biology, systems biology, nanobiotechnology, and information technology.

8. **Products of synthetic biology are often made using multiple techniques of synthetic biology and "conventional" biotechnology more broadly. The majority of current and near-term commercial and industrial applications of synthetic biology use synthetic DNA-circuits and synthetic metabolic pathway engineering to create microbes that produce molecules for**

pharmaceuticals, fuels, chemicals, flavorings and fragrances. The following areas of research are commonly considered "synthetic biology": DNA-based circuits, synthetic metabolic pathway engineering, genome-level engineering, protocell construction, and xenobiology. Some see the insertion of synthetically designed and produced DNA sequences or pathways into an existing genome largely as rebranding conventional biotechnology. Others consider the building of non-natural pathways that would be difficult to achieve with traditional genetic engineering and the *systematic* engineering circuits and pathways as approaches novel to synthetic biology and distinct from traditional genetic engineering.

9. **DNA-based circuits** involve the rational design of sequences of DNA to create biological circuits with predictable, discrete functions, which can then be combined in modular fashion in various cell hosts. Genetic circuits are seen to function as electronic logic components, like switches and oscillators. The idea of interchangeable, discrete parts that can be combined in modular fashion is "one of the underlying promises of the whole approach of synthetic biology."

10. **Synthetic metabolic pathway engineering** aims to redesign or rebuild metabolic pathways, to synthesize a specific molecule from the "cell factory." A synthetic pathway (rationally designed or based on a natural sequence but computer 'optimized') is added to the cell, and then conventional metabolic engineering tools may be used to increase the desired output. Some claim that the aim to *systematically* engineer metabolic interactions sets it apart from conventional metabolic engineering. It can also be seen as different in that synthetic biology tools make it possible to build non-natural pathways that would be difficult to produce with traditional genetic engineering techniques.

11. **Genome-level engineering** focuses on the genome as the "causal engine" of the cell. Rather than designing short DNA sequences or engineering for specific metabolic pathways, researchers work at the whole-genome level, albeit often aiming to produce a "minimal genome." There are two strategies to genome-level engineering: top down and bottom up. **Top-down genome-engineering** starts with a whole genome, from which researchers gradually remove "non-essential" genes to pare down to the smallest possible genome size at which the cell can function as desired. The primary goal is to craft a simplified "chassis" to which modular DNA "parts" can be added. The smaller genome is meant to reduce cellular complexity and thus the potential for unexpected interactions. **Bottom-up genome-engineering** aims to build functional genomes from pieces of synthesized DNA; it is also referred to as "synthetic genomics." Thus far, this has been accomplished with viruses, a 1.08 million base pair bacterial genome, and a chromosome of a yeast genome. At this point, natural genomes are needed as models because of the many DNA sequences that are necessary but have unknown functions.

12. **Protocell construction** aims to create the simplest possible components to sustain reproduction, self-maintenance and evolution. Thus this research seeks to design for less complexity at the *cellular* level (rather than at the genome as in the case of genome-level engineering). This is understood to require three things: a container or membrane to confine reactions; a metabolism so that energy can be stored; and molecules to carry information in order to adapt to changing environments. Research is aiming to achieve compartmentalization through approaches such as lipid-based vesicles, inorganic nanoparticle based membrane vesicles, and membrane-free peptide/nucleotide droplet formation. "Cell-free approaches" attempt to do away with the cell altogether to provide a more controllable biochemical context for synthetic biology devices.

13. **Xenobiology** (also known as chemical synthetic biology) is the study of unusual life forms based on biochemistry not found in nature. Xenobiology aims to alter the "biochemical building blocks of life," such as by modifying genetic information to produce XNA (xeno-nucleic acids) or by producing novel proteins. Xenobiology is often cited as a potential "built-in" biosafety mechanism to prevent genetic drift to wild organisms. Physical genetic material transfer might still occur, but in theory natural polymerases would be unable to accurately "read" the XNA, and thus not lead to protein production. This goal is often described as producing "orthogonal" systems, where modifying one component does not result in side effects to other components in the system. Orthogonality is a foundational property of engineering, and

synthetic biologists are attempting to achieve its expression within living systems. By operating on an orthogonal system, the idea is that synthetic biology devices would be insulated from the rest of the cell's processes and prevent the transfer of parts resulting from synthetic biology to natural biological systems. This claim, however, is untested as xenobiology is in early stages of development.

14. **Although many of the most highly anticipated results of synthetic biology are speculative, synthetic biology techniques are producing current and near-term commercial products and industrial processes.** The global synthetic biology market was estimated to be $1.1 billion in 2010, and predicted to be $10.8 billion by 2016. This market includes products for practicing synthetic biology techniques, such as commercially-available stretches of synthesized DNA and the BioBrick™ Assembly Kit, as well as products produced using synthetic biology techniques. Most of the current and near-term commercial products that are described as resulting from synthetic biology deploy synthetic DNA-circuits and/or synthetic metabolic pathway engineering to modify micro-organisms, intended to be contained in industrial settings, which then produce desired outputs. These outputs include fuels such as biodiesel and isobutanol, organic chemicals, bioplastics, flavor and fragrance molecules, cosmetics and personal care products, and pharmaceuticals. Organisms resulting from synthetic biology techniques are also commercially available, mostly as micro-organisms marketed to industrial producers. Multi-cellular organisms such as plants engineered with synthetic biology techniques for biofuel production seem to be near-term, while the "Glowing Plant" team used Kickstarter to collect funds for the production of plants that will be transformed with synthetically produced DNA and are scheduled to be disseminated in September 2014.

B. Potential positive and negative impacts on the conservation and sustainable use of biological diversity

15. **Synthetic biology could provide more efficient and effective tools to respond to modern challenges, such as responding to biosecurity threats and diagnosing and treating diseases. Current, near-term and anticipated applications of synthetic biology in areas such as bioenergy, environment, wildlife, agriculture, chemical production, biosecurity, and health will have direct impacts specific to each application.** Some of these applications are anticipated to specifically target the conservation and use of biodiversity, either with intended positive impacts (for example, greener industrial processes, de-extinction, bioenergy) or with intended negative impacts (for example, bioterror). Unintentional but direct harm might be experienced, for example if medicines and therapies resulting from synthetic biology techniques trigger unanticipated adverse effects on human health or if synthetic biology laboratory workers are accidentally exposed to components or organisms.

16. **Current and near-term applications of synthetic biology are mostly intended for contained use in research labs and industrial settings. Under these circumstances they are mostly not seen as raising biosafety concerns different from conventional genetic engineering.** Biosafety concerns regarding unintentional releases of these organisms, such as yeast engineered to produce the active ingredient of a natural antimalarial or a bacteria engineered to produce an industrial solvent, are largely not seen as different from those related to conventionally genetically-modified organisms. Some ecologists note that, as micro-organisms have a high potential for evolutionary change, even ones that are unlikely to survive outside of contained use may evolve to become more successful in the environment, and thus represent a potential biosafety concern. Also, some multicellular organisms resulting from techniques that may be considered as synthetic biology intended for environmental release are in near-term production and anticipated for a variety of uses, including crops engineered for efficient conversion into biofuel and insects designed to control pest populations.

17. **Potential future applications of synthetic biology that could provide benefits for the conservation and sustainable use of biodiversity – micro-organisms designed for bioremediation, to enhance agricultural efficiency, to halt desertification, to cure wildlife diseases, etc. – would require the environmental release of micro-organisms resulting from synthetic biology techniques. These**

products involve the deliberate environmental release of organisms modified for specific purposes, and therefore raise different biosafety concerns than those of organisms engineered for contained uses. Since the 1980s, genetically engineered strains of micro-organisms have failed to survive in indigenous microbial communities. If synthetic biology succeeds in producing sufficiently hardy micro-organisms, they could present new biosafety concerns through their potential to transfer synthetic DNA, adapt and evolve to new environments, and impact other organisms in the ecosystem. The ability to address these concerns is constrained by our comparatively limited understanding of these processes in micro-organisms as opposed to multicellular organisms.

18. **If applications of synthetic biology significantly expand in production, this could lead to significant environmental impacts, both intended and unintended.** For example, biofuel production, a significant focus of synthetic biology research, could lead to a shift in global reliance from fossil fuels to biomass, with the intention of cutting harmful greenhouse gas emissions. Such a significant additional demand on global biomass sources, however, may lead to unsustainable extraction from agricultural lands and natural ecosystems and displace traditional users of biomass. After considering the impacts of indirect land-use change and other factors, the net effect on greenhouse could be positive or negative. Particularly considering that many proposed applications of synthetic biology would involve deliberate environmental release, some commentators have noted the need for biologists and others familiar with the complexities of ecosystems to engage with synthetic biology projects.

19. **Considering the current status of commercialization and application, existing regulatory regimes and risk assessment methodologies for genetically modified organisms and living modified organisms may be sufficient in most cases of current products and organisms of synthetic biology. As synthetic biology develops, this assessment will need to be revisited.** Some techniques, such as the use of a gene gun to insert synthetic DNA, do not trigger a regulatory response in some jurisdications. Some believe that synthetic biology techniques are already advanced enough to necessitate such a reassessment. Synthetic biology techniques can be used to insert hundreds or thousands of traits from different donor organisms, which then interact with each other, challenging assessments based on assessing the risks of comparable counterparts of donor and parent organisms, although currently commercialized organisms largely do not utilize such a full range of complexity. Some researchers reflect a concern for the "unknown unknowns" of synthetic biology in their call for significantly increased funding for dedicated synthetic biology risk research. They argue that no one yet understands the risks that synthetic organisms pose to the environment, what kinds of information are needed to support rigorous assessments, or who should collect such data.

20. **There is debate over the degree and probability of harm that organisms resulting from synthetic biology techniques intended for contained use could cause if released.** There is a low probability that synthetic biology organisms which were engineered for contained use and which are released accidentally could survive and propagate. On the other hand, the majority of research in synthetic biology uses microbes as hosts which have a particularly high potential for mutations. Once released into the environment these organisms cannot be retrieved and could potentially represent a catastrophic risk. Such a low-probability and high-consequence situation raises ethical issues around harms, benefits and risks.

21. **Among synthetic biologists and in policy discussions, a commonly suggested response to the limitations of physical containment and the possibility of organisms successfully designed for environmental release is that synthetic biology be used to design organisms with "built-in safety features."** Some of these strategies to engineer biosafety rely on xenobiology, the replacement of the genetic alphabet of DNA with novel informational biopolymers or with unnatural base pairs which are not expected to be able to interact with natural forms of life on the genetic level. Although promising, the science of xenobiology is not yet able to demonstrate containment, and significant research challenges remain.

22. **If research in synthetic biology develops as many anticipate – or if current commercial and industrial applications of synthetic biology expand in scale – synthetic biology could cause manufacturing and economic paradigm shifts.** Synthetic biology could be a key technology in developing economies in which biotechnology contributes a significant share or economies using biological resources and bio-based processes. How developing countries would fare in such a global "bioeconomy" is not self-evident. Synthetic biology could benefit the health and economies of developing countries through specific applications, and the tropics and sub-tropics could be major sources of the biomass needed as feedstock for bio-based processes. It is also possible that a biotechnology-led bioeconomy could reinforce inequitable trends in international trade, that the scale of extraction and use of biomass for a global bioeconomy could be ecologically unsustainable and threaten traditional economies reliant on biomass, and that natural products currently grown or harvested will be displaced by industrial production from micro-organisms resulting from synthetic biology techniques. The shape of new bioeconomies and the fates of their ecological and human communities can be influenced by government regulations and economic instruments.

23. **Ethical issues are invoked by specific applications of synthetic biology and, more generally, synthetic biology techniques.** Specific applications of synthetic biology such as "de-extinction" projects raise ethical issues such as how best to weigh and balance a project's potential harms and benefits, how limited resources for conservation should be directed, and whether support for *in situ* conservation might be seen as less pressing due to the expectation that 'lost' species can be resurrected. More broadly, the increased capabilities of synthetic biology techniques raise ethical issues. Ethicists debate whether we have already crossed the threshold from the modification of existing organisms to the creation of *de novo* organisms, and what the ethical implications of this might be. How should such new organisms be valued? Does synthetic biology move humanity towards instrumentalism, by which organisms are assigned value based on their instrumental use? Could this influence the ethical basis for conservation, or influence public perceptions of what is "natural"? Like other biotechnologies, synthetic biology raises ethical questions around the level of predictability of its positive and negative impacts that should be required, and how to weigh anticipated impacts and the possibility of unexpected impacts.

24. **Intellectual property right regimes are still developing around synthetic biology, and could impact the development of the field and specific applications.** Two main models of intellectual property for synthetic biology components, organisms, products, and techniques seem to be forming: heavy reliance on patents and a system modeled on open-source software that enables a combination of patenting and shared use of designed DNA sequences. Depending on the intellectual property rights regimes, innovation in synthetic biology may be encouraged, stifled, or directed towards certain kinds of applications or users.

C. Possible gaps and overlaps with the applicable provisions of the Convention, its Protocols and other relevant agreements

1. Overview

25. **Synthetic biology as such has not been addressed in the text of multilateral treaties. However, a multitude of treaties, customary rules and general principles of law, as well as other regulatory instruments and mechanisms, could apply to all or some forms of what has been described as synthetic biology.** Most of these treaties were developed before synthetic biology was a significant issue and, as such, only in a few cases contain explicit references to components, organisms and products resulting from synthetic biology techniques and their potential impacts. Depending on the circumstances, existing treaties may address: the transfer and handling of components, organisms and products resulting from synthetic biology techniques; the use of components, organisms and products resulting from synthetic biology techniques for a specific purpose, in particular for hostile purposes or in armed conflict; the rights associated with components, organisms and products resulting from synthetic

biology techniques, e.g. patentability; and access to genetic resources used in synthetic biology techniques, and sharing of benefits arising from their utilization.

2. General rules of customary international law and treaties addressing the potential risks arising from the application of synthetic biology techniques

26. **State responsibility describes the rules governing the general conditions under which a State is responsible for wrongful actions or omissions, and the resulting legal consequences.** The rules on State responsibility require a breach of an obligation without defining these obligations. They provide only a general framework for addressing breaches of international law, including customary rules of international law and treaty obligations. The rules on State responsibility therefore do not address the conditions under which synthetic biology techniques would be permitted or prohibited. Under the rules on State responsibility, States are not as such responsible for acts by private actors unless one of the recognized relationships exists. However, a State might have to address the actions of private actors in order to fulfil its own obligation. A State could be in breach of an obligation if it fails to take necessary measures to prevent effects caused by private actors.

27. **States are under a general obligation to ensure that activities within their jurisdiction or control respect the environment of other States or of areas beyond national jurisdiction or control.** This duty to respect the environment does not mean, however, that *any* environmental harm, pollution, degradation or impact is generally prohibited. The duty prohibits a State from causing *significant transboundary* harm and obliges a State of origin to take adequate measures to control and regulate in advance sources of such potential harm. States have to exercise "due diligence" before carrying out potentially harmful activities. What constitutes "due diligence" would largely depend on the circumstances of each case. Establishing State responsibility for any harm from a synthetic biology technique would require that (i) the application of a synthetic biology technique can be attributed to a particular State and (ii) that it can be associated with a significant and particular harm to the environment of other States or of areas beyond national jurisdiction or control.

28. **States have the duty to carry out an environmental impact assessment for activities that may have a significant adverse impact in a transboundary context, in particular, on a shared resource.** An environmental impacts assessment (EIA) is required in many domestic legal orders and the International Court of Justice has recently recognized that the accepted practice among States amounts to "a requirement under general international law". Thus, where there is a risk that a proposed industrial activity may have a significant adverse impact in a transboundary context, the requirement to carry out an environmental impact assessment applies even in the absence of a treaty obligation to this effect.

29. **The precautionary principle or approach is relevant but its legal status and content in customary international law has not been clearly established, and the implications of its application to synthetic biology techniques are unclear.** There is no uniform formulation or usage for the precautionary approach and its legal status in customary international law has not yet been clearly established, although it has been invoked several times by some States. The precautionary approach is understood to state, as a minimum, that scientific uncertainty should not be used as a reason to postpone action. Further interpretations include that "uncertainty justifies action", or even that it implies a duty of states to take action for responding to a given environmental risk.

30. **Many components, organisms and some products resulting from synthetic biology techniques may be considered as "living modified organisms resulting from biotechnololgy" as defined by the Convention on Biological Diversity and be subject to its biosafety provisions (Articles 8(g) and 19).** While its provisions on biosafety address potential negative impacts, the Convention also recognizes potential positive effects of modern biotechnology and provides for the access to and transfer of technologies, including biotechnology, that are relevant to the conservation and sustainable use of biological diversity. Where LMOs resulting from synthetic biology techniques are

likely to have adverse environmental impacts that could affect the conservation and sustainable use of biological diversity, taking also into account the risks to human health, Parties are required to establish or maintain means to regulate, manage or control these risks at the national level. In addition, the Convention contains information sharing requirements for exporting countries.

31. **Organisms resulting from synthetic biology techniques may fall under the definition of "living modified organisms" under the Cartagena Protocol for Biosafety. Therfore, its requirements pertaining to the transboundary movement, transit, handling and use of all living modified organisms that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, may apply.** In many cases components, organisms and products resulting from synthetic biology techniques could fulfil the criteria of (i) being a living organism, (ii) possessing a novel combination of genetic material, and (iii) resulting from the use of modern biotechnology. While a number of applications of synthetic biology techniques are intended to result in pharmaceuticals for humans, those pharmaceuticals have so far not been addressed by other relevant international agreements or organizations, and therefore do not trigger an exemption from the provisions of the Cartagena Protocol. Some components, organisms and products resulting from synthetic biology techniques may fall under exemptions from the Advanced Informed Agreement provisions for LMOs, if they are intended for contained use or for direct use as food or feed, or for processing, which may raise biosafety concerns. Although LMOs produced through synthetic biology may present characteristics that are not common to all LMOs, Annex III of the Protocol on risk assessment, including its general principles, points to consider and methodology are still fully applicable to living organisms produced through synthetic biology and may also apply to "products thereof" that contain "detectable novel combinations of replicable genetic material obtained through the use of modern biotechnology".

32. **The Conference of the Parties, in decision XI/11 explicitly addressed the matter of synthetic biology and, recognizing the development of technologies associated with synthetic life, cells or genomes, and the scientific uncertainties of their potential impact on the conservation and sustainable use of biological diversity, urged Parties and invited other Governments to take a precautionary approach, in accordance with the preamble of the Convention and with Article 14, when addressing threats of significant reduction or loss of biological diversity posed by organisms, components and products resulting from synthetic biology, in accordance with domestic legislation and other relevant international obligations.** In its decisions addressing biofuels, the Conference of the Parties also urged Parties and other Governments to apply the precautionary approach to the introduction and use of living modified organisms for the production of biofuels as well as to the field release of synthetic life, cell, or genome into the environment, and to monitor technology associated with biofuels. In case components, organisms and products resulting from synthetic biology techniques become invasive, existing guidance from the Conference of the Parties on invasive alien species could apply, as far as they are "living", able to reproduce, and have a "natural distribution".

33. **Once entered into force, the Nagoya–Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol on Biosafety will require Parties to provide at the national level for rules and procedures that address damage from living modified organisms resulting from synthetic biology techniques**, where such damage falls under the definition set out in Article 2 of the Supplementary Protocol.

34. **The Biological Weapons Convention addresses, in part through legally-binding rights and obligations, microbial or other biological agents or toxins, including those which are components, organisms and products resulting from synthetic biology techniques, and provides a forum where further guidance for this aspect of synthetic biology could be developed.** Parties to the Convention have confirmed that certain components, organisms and products resulting from synthetic biology techniques fall under the scope of "microbial or other biological agents, or toxins whatever their origin or method of production", which the Convention regulates. Where those agents or toxins are "of types and in

quantities that have no justification for prophylactic, protective or other peaceful purposes", the Convention, among others: (i) prohibits that its parties develop, produce, stockpile or otherwise acquire or retain them; (ii) requires its Parties with those agents or toxins in their possession or under their jurisdiction or control, to destroy, or to divert them to peaceful purposes, (iii) prohibits their transfer; (iv) prohibits assisting, encouraging, or inducing any State, group of States or international organizations to manufacture or otherwise acquire them; and (v) requires its parties to take necessary measures at the national level. In addition, the convention contains the obligation to facilitate, and the right to participate in, the fullest possible exchange of equipment, materials and scientific and technological information, where they are used for peaceful purposes. Different meetings of the Parties to the Convention have acknowledged the potential positive and negative impacts from, among others, synthetic biology, and agreed on the value of promoting appropriate oversight measures to identify and manage risks, exploring approaches for developing guiding principles that could be tailored to national circumstances, sharing information about oversight frameworks, guiding principles, and practical experience, and the elaboration of models to inform risk assessment and oversight of scientific research activities that have significant dual-use potential, while promoting access to, and use of, the technologies they reviewed, including through the development of inexpensive and field-portable applications.

35. **Some components, organisms and products resulting from synthetic biology could, depending on the specific case, be considered as causing risks to animal or plant life or health arising from the entry, establishment or spread of pests, diseases, disease-carrying organisms or disease-causing organisms; or as risks to human or animal life or health arising from additives, contaminants, toxins or disease-causing organisms in foods, beverages or feedstuffs. If this is the case, members of the World Trade Organization can adopt and enforce sanitary and phytosanitary measures in accordance with the provisions of the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement).** The measures could directly or indirectly affect international trade, as long as they are taken in accordance with standards recognized under the SPS Agreement. The SPS Agreement explicitly recognizes the international standards, guidelines and recommendations developed by three organizations: For food safety the Codex Alimentarius Commission; for animal health and zoonoses the relevant international standards, guidelines and recommendations developed by the World Organisation for Animal Health (OIE); for plant health, those developed by the International Plant Protection Convention (IPPC). In particular, components, organisms and products resulting from synthetic biology may be intentionally or unintentionally released to the environment, leading to biosafety concerns. Depending on the circumstances, they could be considered to pose risks to animal or plant life or health, through ecosystem-level impacts or the transfer of synthetic DNA. While guidance exists as to the application of standards to living modified organisms, it is not clear for all forms of synthetic biology techniques how these standards could be applied. The standard-setting organizations Codex Alimentarius Commission, World Organisation for Animal Health (OIE) or International Plant Protection Convention (IPPC) have not explicitly addressed synthetic biology.

3. Treaties addressing access to genetic resources, benefit-sharing from their utilization, and intellectual property rights that could be relevant to the application of synthetic biology techniques

36. **In the cases where synthetic biology requires access to genetic resources, the access requirements of the Convention would, in general, apply and thus require prior informed consent (unless otherwise determined) and the negotiation of mutually agreed terms.** However, there are cases, such as virtual/digital information on functional units of heredity, where it is not clear that the material accessed for its use in synthetic biology can be considered "genetic resources" in accordance with the definitions contained in Article 2 of the Convention. It is also unclear whether the components, organisms and products resulting from synthetic biology can be considered "genetic resources" under the Convention.

37. **Generally, some synthetic biology techniques can be considered as a way of "utilizing" genetic resources within the context of the Nagoya Protocol.** The definition of utilization contained in the Nagoya Protocol can help to determine which activities related to synthetic biology would be within the scope of the Protocol. The use of synthetic biology techniques opens questions regarding the extent to which the results of modifications of natural genetic resources continue to be subject to the benefit-sharing obligations under the Nagoya Protocol. Synthetic biology also raises a number of questions in relation to derivatives and the application of the Nagoya Protocol. There are different interpretations regarding how the Nagoya Protocol applies to derivatives. National implementation of the Nagoya Protocol can assist in further clarifying the scope of access and benefit-sharing requirements in relation to derivatives. The negotiation of mutually agreed terms can assist parties to an access and benefit-sharing agreement to clarify to which extent of the value chain the obligations to share benefits would continue to apply to components, organisms and products resulting from synthetic biology, including derivatives and their subsequent applications.

38. **The International Treaty on Plant Genetic Resources for Food and Agriculture may be particularly relevant to synthetic biology with regard to the access to genetic resources for use in synthetic biology processes and the sharing of the benefits arising from commercialization.** Its Article 12 requires parties to provide facilitated access to plant genetic resources for food and agriculture to other parties, including to legal and natural persons under their jurisdiction. This access is to be granted pursuant to a standard material transfer agreement (MTA) through the Multilateral System under certain conditions. Synthetic biology research that does not include chemical, pharmaceutical and/or other non-food/feed industrial uses can access, in accordance with the relevant provisions of ITPGRFA, the plant genetic resources for food and agriculture listed in Annex I to the Treaty, a pool of 64 food and forage crops. These plant genetic resources cannot be protected through an intellectual property right in the form received from the Multilateral System. Under Article 13 of ITPGRFA Parties agreed that benefits arising from the use, including commercial, of plant genetic resources for food and agriculture under the Multilateral System shall be shared fairly and equitably through the exchange of information, access to and transfer of technology, capacity-building, and the sharing of the benefits arising from commercialization.

39. **It appears that for the present, in accordance with the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS Agreement), patents could be available under national law of WTO members for most of the current products and all of the techniques (to the extent that they are all "non-biological" in the sense of being "technical). Select products of synthetic biology techniques may fall under the exceptions provided by Article 27, paragraphs 2 and 3 of the TRIPS Agreement and may therefore be excluded from patentability by some WTO members.** The patentability of synthetic biology products and techniques may have both positive and negative implications, as it may encourage research and investments into, and restrict access to, and application of, both technologies with potentially positive and potentially negative implications for biodiversity. The possibility to exclude certain synthetic biology products and techniques from patentability if necessary to protect *ordre public* or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, in accordance with Article 27, paragraphs 2 of the TRIPS Agreement may help to avoid some negative effects that may result from synthetic biology techniques.

40. **The results of current synthetic biology research that is focused on modifying existing "natural" genomes could qualify as "essentially derived varieties" and therefore be protected by the "breeder's right" (a *sui generis* form of protection for intellectual property rights on plant varieties) under the International Convention for the Protection of New Varieties of Plants (UPOV Convention).** For essentially derived varieties, both the breeder of the initial variety, from which the essentially derived variety is derived, and the breeder of the essentially derived variety would enjoy a breeder's right. As far as synthetic biology research may someday result in the production of entirely novel genomes, it may be able to produce new plant varieties which could be protected by the breeder's right. Where a breeding process draws upon a protected variety and results in a new plant variety, the

breeder of the new variety, on an exceptional basis, would not require the authorization of the breeder of the initial variety.

4. Gaps in the current regulatory framework

41. **Some general principles of international law such as the duty to avoid transboundary harm, and the need to conduct an environmental impact assessment (EIA), together with the rules of State responsibility may provide some guidance relevant to addressing potential negative impacts resulting from the application of synthetic biology techniques, but would still form an incomplete basis to address all potential negative impacts.** Uncertainties exist with regard to their application in the absence of decision-making institutions or specific guidance. In addition, they may not be able to address the scope of the risks associated with some forms of synthetic biology techniques. Specific potential impacts of specific synthetic biology products might violate particular rules, but this cannot be determined unless there is greater confidence in estimates of such potential impacts.

42. **Potential gaps may exist with regard to components, organisms and products resulting from synthetic biology techniques that are not living modified organisms.** Such gaps could occur where components, organisms and products resulting from synthetic biology techniques do not fall within the scope of a treaty regime. For example, components, organisms and products resulting from synthetic biology techniques that are not living modified organisms will not be subject to the requirements pertaining to the transboundary movement, transit, handling and use of all living modified organisms that may have adverse effects on the conservation and sustainable use of biological diversity contained in the Cartagena Protocol, nor the provisions on liability and redress contained in the Nagoya – Kuala Lumpur Supplementary Protocol.

43. **A number of treaties exist which, in general, provide for mechanisms, procedures or institutions that could address potential negative effects associated with the application of synthetic biology techniques, but where no specific guidance exists for their application.** For example, States may be able to establish import restrictions on components, organisms and products resulting from synthetic biology techniques in accordance with the SPS Agreement. However, while specific guidance has been developed for the application of standards to living modified organisms, for example under the International Plant Protection Convention (IPPC), no such guidance exists for other components, organisms and products resulting from synthetic biology techniques.

44. **The international regulatory framework is not well equipped to address the potentially "catastrophic" and "existential" risks, with low and very low probability, but immense impacts, that are discussed in the context of some synthetic biology techniques, with the exception of the Biological Weapons Convention, which prohibits the development, acquisition and transfer of microbial or other biological agents for non-peaceful purposes.** Most regulatory mechanisms discussed in the report were developed before synthetic biology was a significant issue and therefore they were not intended to cope with the scope and scale that some of the potential impacts of synthetic biology may have. The only exception is the Biological Weapons Convention, which prohibits that its parties develop, produce, stockpile or otherwise acquire or retain microbial or other biological agents or toxins of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes. While some treaties include frameworks for risk assessment, sufficient information may not be available for all synthetic biology techniques to effectively conduct risk assessments.

45. **In sum, the current regulatory mechanisms that could apply to synthetic biology techniques and the components, organisms and products resulting from them would not address all potential positive and negative impacts.** While the mandate of some treaties or institutions is sufficiently broad to address some or all synthetic biology techniques, there is no mechanism to ensure that the issues are actually addressed in a consistent and comprehensive manner.

III. APPLICATION OF CRITERIA FOR NEW AND EMERGING ISSUES TO SYNTHETIC BIOLOGY

46. In paragraph 12 of decision IX/29, the Conference of the Parties established criteria for identifying new and emerging issues related to the conservation and sustainable use of biodiversity. This section discusses how these criteria apply to the issue of synthetic biology.

A. Relevance of the issue to the implementation of the objectives of the Convention and its existing programmes of work

47. The majority of current and near-term commercial and industrial applications of synthetic biology use synthetic DNA-circuits and metabolic pathway engineering to create microbes that produce molecules for pharmaceuticals, fuels, chemicals, flavourings and fragrances. Synthetic biology techniques are making it possible to engineer microbes to produce molecules that have been naturally-sourced or derived from petroleum. Future applications of synthetic biology are expected in areas such as bioenergy, environment, wildlife, agriculture, chemical production, biosecurity. These current and near-term applications of synthetic biology techniques may have positive and negative impacts on the conservation and sustainable use of biodiversity specific to each application.

48. If only the products resulting from synthetic biology techniques, but not the components and organisms that produce them, are released into the environment, these products may have implications for the environments in which the natural production of these products occurs (i.e. potentially all biomes covered in the thematic programmes of work), but would also result in socio-economic impacts on the production systems (with implications for a range of cross-cutting issues including Articles 8(j) and 10(c), protected areas, sustainable use, access and benefit-sharing, Global Strategy for Plant Conservation, among others).

49. If there is unintended or intended release of the components and organisms resulting from synthetic biology techniques, then there are potential interactions with, and impacts on, species in all biomes and these could potentially have consequences for ecosystem processes, functioning, the delivery of ecosystem services and hence for human well-being as well as potentially affect human health. In addition to programmes of work and cross-cutting issues listed above, impact assessment, risk assessment for living modified organisms, and liability and redress would be relevant to such a release.

50. Components, organisms and products resulting from synthetic biology techniques that may have impacts on the conservation and sustainable use of biological diversity and associated social, economic and cultural considerations also have the potential to influence the achievement of several Aichi Biodiversity Targets and are therefore relevant to the implementation of the Strategic Plan for Biodiversity 2011-2020.

B. New evidence of unexpected and significant impacts on biodiversity

51. Several Parties and organizations, in their submissions responding to notification 2013-018 (Ref. No. SCBD/STTM/DC/RH/VA/81439), dated 22 February 2013, contend that there is no “reliable” or “credible” scientific evidence of impacts of existing components, organisms and products resulting from synthetic biology techniques on the conservation and sustainable use of biodiversity, or that there is insufficient information to analyse their impacts on biodiversity. Some organizations argue, in their submissions, that lack of evidence of impacts is not evidence of a lack of impacts, and that not enough studies have specifically investigated potential impacts of synthetic biology components, organisms and products on biodiversity, such as environmental and human health as well as socio-economic impacts.

52. Some researchers reflect a concern for the “unknown unknowns” of synthetic biology in their call for significantly increased efforts on dedicated synthetic biology risk research. One submission

responding to notification 2013-018 called for capacity-building on the management of risks related to the release of organisms resulting from synthetic biology techniques and asked that this be conveyed to the Global Environment Facility.

53. Current and near-term applications of synthetic biology are mostly intended for contained use in research labs and industrial settings; under these circumstances they are mostly not seen as raising biosafety concerns different from conventional genetic engineering. As micro-organisms have a high potential for evolutionary change, even ones that are unlikely to survive outside of contained use may evolve to survive and reproduce in the environment, and thus represent a potential biosafety concern. If synthetic biology succeeds in producing sufficiently hardy micro-organisms for intentional environmental release, they could present new biosafety concerns through their potential to transfer synthetic DNA, adapt and evolve to new environments, and impact other organisms in the ecosystem. In addition, if applications of synthetic biology significantly expand in production, this could lead to significant environmental impacts, both intended and unintended, for example through land-use changes. Furthermore, "catastrophic" and "existential" risks, with low and very low probability, but immense impacts, are discussed in the context of some synthetic biology techniques.

C. Urgency of addressing the issue/imminence of the risk caused by the issue to the effective implementation of the Convention as well as the magnitude of actual and potential impact on biodiversity

54. The results of genome-level engineering thus far are based on natural genomes, rather than the design of *de novo* organisms. Protocells and xenobiology are likely confined to the laboratory for the near to medium-term. Current organisms resulting from synthetic biology techniques are almost entirely used in contained settings such as laboratories and industrial bioreactors, although there are notable exceptions such as the planned broad dissemination of the Glowing Plant.

55. However, many anticipated applications of synthetic biology involve much greater changes to natural genomes and/or require environmental release of organisms resulting from synthetic biology techniques. It is, however, very hard to predict how soon such techniques will be perfected or when such applications might be considered ready for wider dissemination.

D. Actual geographic coverage and potential spread, including rate of spread, of the identified issue relating to the conservation and sustainable use of biodiversity

56. Academic and industrial research on synthetic biology is occurring throughout the world. Although the core of research occurs in the United States of America and European countries, other sites of major research include Argentina, Brazil, China, India, Mexico, Singapore and South Africa . The vast majority of organisms resulting from synthetic biology techniques are currently in contained use in research labs or industrial settings; it is the *products* of organisms resulting from synthetic biology techniques that are primarily being dispersed commercially. Some larger organisms resulting from synthetic biology techniques are on the cusp of being distributed commercially – primarily the US company Glowing Plants, which is due to distribute seeds and plants within the USA in September 2014. It is unclear whether other near-term multi-cellular applications, such as corn seed engineered to express biodegrading enzymes to aid in ethanol production and transgenic mosquitoes, have used synthetic biology techniques.

57. Synthetic biology is a young field that has experienced rapid growth in the past decade with government and industry support. High expectations have been placed on synthetic biology, but it is impossible to predict how fast or at what rate applications will successfully make the transition from research lab to commercialization.

E. Evidence of the absence or limited availability of tools to limit or mitigate the negative impacts of the identified issue on the conservation and sustainable use of biodiversity

58. In terms of potential negative impacts, tools to limit or mitigate such impacts include the following: national and regional regulatory oversight; multilateral treaties and customary international law and principles; and self-regulation. A number of public national assessments have found that existing regulatory regimes and risk assessment methodologies for genetically modified organisms and living modified organisms are sufficient for current research and applications of synthetic biology. The current international regulatory mechanisms that could apply to synthetic biology techniques and the components, organisms and products resulting from them do not constitute a coherent international legal framework that addresses all potential negative impacts.

59. Many components, organisms and products resulting from synthetic biology techniques may be considered living modified organisms and therefore fall under relevant provisions on their transfer, handling and use provided by a number of multilateral treaties, including the Cartagena Protocol on Biosafety and the Convention's provisions on biosafety. Gaps may exist with regard to components, organisms and products resulting from synthetic biology techniques that are not living modified organisms. Some scholars have questioned whether the risk assessment methodology in Annex III to the Cartagena Protocol on Biosafety is adequate for organisms resulting from synthetic biology techniques that utilize genetic parts from many different donor organisms or that have no natural analogue.

60. Where components, organisms and products resulting from synthetic biology can be considered as causing risks to animal or plant life or health or as risks to human or animal life or health, WTO members have the possibility to adopt and enforce sanitary and phytosanitary measures in accordance with the provisions of the SPS Agreement. While guidance exists as to the application of standards for such measures to living modified organisms, it is not clear for all forms of synthetic biology techniques how these standards could be applied.

61. The international regulatory framework is not well equipped to address the potentially "catastrophic" and "existential" risks, with low and very low probability, but immense impacts, that are discussed in the context of some synthetic biology techniques, with the exception of the Biological Weapons Convention, which prohibits the development, acquisition and transfer of microbial or other biological agents for non-peaceful purposes. The Biological Weapons Convention has not taken concrete steps towards the development of an oversight framework, guiding principles, or models to inform risk assessment and oversight of scientific research.

F. Magnitude of actual and potential impact of the identified issue on human well-being

62. Synthetic biology may already have actual positive and negative impacts on human well-being, like for instance in the treatment of malaria by semi-synthetic artemisinin or unintended exposure of laboratory workers to synthetic biology. These impacts are not yet systematically identified or measured.

63. The potential magnitude of impacts of synthetic biology on human well-being depends in large part on the trajectory of synthetic biology's development. If synthetic biology lives up to expectations, it could have major impacts on aspects of human well-being through specific applications of synthetic biology techniques in areas such as health and biosecurity.

64. Beyond specific applications, synthetic biology techniques raise ethical issues that can be seen as potentially impacting human well-being. Some ethicists have warned that synthetic biology could have dangerous impacts on human ethics, such as undermining the status of living things or changing humanity's attitude and approaches to nature. Others point out that such impacts have not yet been noted,

and are unlikely on the basis of what is actually possible with synthetic biology in its current status (ie, not yet creating *de novo* organisms).

G. Magnitude of actual and potential impact of the identified issue on productive sectors and economic well-being as related to the conservation and sustainable use of biodiversity

65. Synthetic biology is already having impacts on productive sectors and economic well-being; the global synthetic biology market was estimated to be $1.1 billion in 2010, and predicted to be $10.8 billion by 2016. Economic impacts related to conservation and sustainable use of biodiversity, however, are not yet systematically identified or measured.

66. If current applications of synthetic biology expand in scale, they may result in the displacement of naturally grown or harvested products. This could lead to complex trade-offs. Products of synthetic biology applications may deliver benefits to the same communities whose livelihoods have been displaced, and/or may not fully displace pre-existing methods of production. It is also possible that a biotechnology-led bioeconomy could reinforce trends towards the dominance of knowledge-based economies, and the further consolidation of international trade by a few rich States and transnational corporations.

67. The potential magnitude of impacts of synthetic biology on productive sectors and economic well-being related to conservation and sustainable use of biodiversity depends on the trajectory of synthetic biology's development. Numerous state-led policies and strategies are driven by the anticipated benefits of an expanded global bioeconomy. Engagement by some civil society groups on synthetic biology is significantly motivated by anticipated dangers of an expanded global bioeconomy, such as ecologically unsustainable extraction and use of biomass.

IV. SUGGESTED RECOMMENDATIONS

The Subsidiary Body on Scientific, Technical and Technological Advice may wish to adopt a recommendation along the following lines:

The Subsidiary Body on Scientific, Technical and Technological Advice,

Having taken note of the information compiled by the Executive Secretary on synthetic biology and its potential impacts on biodiversity and on the possible gaps and overlaps with the Convention, its Protocols and other relevant agreements (UNEP/CBD/SBSTTA/18/INF/3 and INF/4) and having considered the application of the criteria for new and emerging issues to the field of synthetic biology, *notes* that:

(a) Synthetic biology may be understood to involve various techniques, organisms and components and result in a range of products, living and non-living, and of differing characteristics;

(b) Some of these techniques, organisms and components have already resulted in commercial products and industrial processes, others are expected to in the near-term, while yet others have a potential in the longer-term or are speculative;

(c) There are a number of intended benefits of these products and processes;

(d) There are also risks associated with the components, organisms and products resulting from synthetic biology techcniques, some expected and manageable, some involving a high degree of uncertainty and others unforeseeable;

(e) There is no coherent international regulatory framework for synthetic biology techniques and the components, organisms and products resulting from them;

(f) There is uncertainty regarding the adequacy of existing national and international regulatory regimes and risk assessment methodologies for components, organisms and products resulting from synthetic biology techniques.

Recommendation to the Conference of the Parties

The Subsidiary Body on Scientific, Technical and Technological Advice *recommends* that the Conference of the Parties, at its twelfth meeting, adopt a decision along the following lines:

The Conference of the Parties

1. *Urges* Parties and other Governments:

(a) To approve organisms resulting from synthetic biology techniques for field testing only with appropriate scientific data to justify such testing;

(b) To approve organisms resulting from synthetic biology techniques for commercial use only after appropriate, authorized and strictly controlled scientific assessments with regard to their potential ecological and socio-economic impacts and any adverse effects for biological diversity, food security and human health have been carried out in a transparent manner and the conditions for the safe and beneficial use of these organisms have been validated;

(c) To have effective procedures and regulatory processes in place that govern the approval processes under (a) and (b) above;

2. *Invites* Parties, other Governments, relevant international organizations, indigenous and local communities, and other stakeholders:

(a) To report on measures undertaken in accordance with paragraph 1 above, and to submit such information to the Executive Secretary;

(b) To provide further information on potential and actual impacts of synthetic biology on the conservation and sustainable use of biological diversity and associated social, economic and cultural considerations as well as on existing regulatory frameworks and gaps in these;

3. *Requests* the Executive Secretary to make available the information reported in accordance with paragraph 2 above through the clearing-house mechanism of the Convention and other means.
