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Item 24 of the provisional agenda[*]

SYNTHETIC BIOLOGY: UPDATED REPORTS

Note by the Executive Secretary

INTRODUCTION

1. In decision XI/11, 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:

(a) To 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) To compile and synthesize relevant available information, together with the accompanying information;

(c) To 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;

[*] UNEP/CBD/COP/12/1/Rev.1.

(d) To 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 documents were made available for the information of the Subsidiary Body as information documents UNEP/CBD/SBSTTA/18/INF/3 and INF/4, and the key messages were made available in document UNEP/CBD/SBSTTA/18/10.

5. The Subsidiary Body, at its eighteenth meeting, considered the key messages and adopted recommendation XVIII/7 on new and emerging issues: synthetic biology, including a draft decision for consideration of the Conference of the Parties at its twelfth meeting. Recommendation XVIII/7 requested the Executive Secretary to provide additional opportunities for peer-review of the information documents referred to in paragraph 4 above and to make updated documents available prior to the twelfth meeting of the Conference of the Parties.

6. In response to this request, the Executive Secretary issued notification 2014-090 (Ref. No. SCBD/SAM/DC/SS/AC/83708), dated 4 July 2014, inviting Parties and relevant organizations to further review the documents. Comments were received from 11 Parties, 19 organizations, and one submission from an independent expert.The documents have been revised taking into account the peer-review comments and are presented in information documents UNEP/CBD/COP/12/INF/11 and UNEP/CBD/COP/12/INF/12. The present note contains the key messages of the revised documents on the potential positive and negative impacts on the conservation and sustainable use of biological diversity and associated social, economic and cultural considerations (section II), and on possible gaps and overlaps with the applicable provisions of the Convention, its Protocols and other relevant agreements (section III). This document is made available for the information of Parties to the Convention and is not intended to affect the rights and obligations of Parties to the Convention or its Protocols.

7. The draft decision, as contained in recommendation XVIII/7 of the Subsidiary Body on Scientific, Technical and Technological Advice, is made available in the compilation of draft decisions for the Twelfth Meeting of the Conference of the Parties to the Convention on Biological Diversity.[1]

I. AREAS OF RESEARCH AND APPLICATIONS COMMONLY CONSIDERED TO BE SYNTHETIC BIOLOGY

8. **Synthetic biology falls within the scope of biotechnology, as defined by the Convention on Biological Diversity i.e. "... any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use."** Synthetic biology methodologies and techniques share various degrees of overlap with those of "modern biotechnology" and, in particular, the "application of *in vitro* nucleic acid techniques […] that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection" as defined in the Cartagena Protocol on Biosafety.

9. **While there is no internationally agreed definition of "synthetic biology", key features of synthetic biology include the "*de novo*" synthesis of genetic material and an engineering-based approach to develop components, organisms and products.** Synthetic biology builds on modern biotechnology methodologies and

[1] UNEP/CBD/COP/12/1/Add.2.

techniques such as high throughput DNA technologies and bioinformatics. There is general agreement that the processes of synthetic biology aim to exercise control in the design, characterization and construction of biological parts, devices and systems to create more predictable biological systems. The areas of research that are considered "synthetic biology" include DNA-based circuits, synthetic metabolic pathway engineering, synthetic genomics, protocell construction, and xenobiology:

(a) **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 in a manner analogous to electronic logic components, like switches and oscillators;

(b) **Synthetic metabolic pathway engineering** aims to redesign or rebuild metabolic pathways, to synthesize a specific molecule from the "cell factory." A synthetic pathway (typically based on naturally occurring DNA sequences that are computer 'optimized') is added to the cell, and then classic genetic engineering tools may be used to increase the desired output;

(c) **Synthetic genomics** focuses on the genome as the "causal engine" of the cell. Top-down synthetic genomics 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. Bottom-up synthetic genomics aims to build functional genomes from pieces of synthesized DNA. At this point, natural genomes are needed as models because of the many DNA sequences that are necessary but have unknown functions;

(d) **Protocell construction** aims to create the simplest possible components to sustain reproduction, self-maintenance, metabolism and evolution. Thus this research seeks to design for less complexity at the *cellular* level (rather than at the genome level as in the case of genome-level engineering);

(e) **Xenobiology** (also known as chemical synthetic biology) is the study and development of life forms based on biochemistry not found in nature. Xenobiology aims to alter DNA and RNA to produce XNA (xeno-nucleic acids) and novel proteins. Xenobiology is often cited as a potential "built-in" biocontainment mechanism to prevent gene transfer to wild organisms.

10. **Current and near-term commercial and industrial applications of synthetic biology aim at creating micro-organisms that synthesise products for fuels, pharmaceuticals, chemicals, flavorings and fragrances.** The majority of these applications of synthetic biology engineer microbes, such as the frequently-used *E. coli*, baker's yeast (*Saccharomyces cerevisiae*) and microalgae, to produce alternatives to naturally-occurring or petroleum-based molecules. One such example is the production of artemisinic acid in engineered yeast with the aim of manufacturing an alternative to the naturally occurring anti-malarial drug artemisinin, which is derived from *Artemisia* plants. Another example is the production of fuels such as biodiesel and isobutanol using synthetic biology techniques. Synthetic biology techniques are also being explored and used for the production of pharmaceutical drugs (e.g. to lower blood sugar levels in adults with type 2 diabetes) and flavourings/fragrances (e.g. vanillin). Although many of the anticipated results of synthetic biology are highly speculative, synthetic biology, in combination with modern biotechnology techniques, is 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.

II. POTENTIAL POSITIVE AND NEGATIVE IMPACTS ON THE CONSERVATION AND SUSTAINABLE USE OF BIOLOGICAL DIVERSITY AND ASSOCIATED SOCIAL, ECONOMIC AND CULTURAL CONSIDERATIONS

11. **Components, organisms and products of synthetic biology may have some positive impacts on the conservation and sustainable use of biodiversity.** Many of the applications of synthetic biology aim at developing more efficient and effective ways to respond to challenges associated with bioenergy, environment, wildlife, agriculture, health and chemical production. Potentially, positive impacts may be realized in a number of ways, including, for example:

(a) The development of micro-organisms designed for bioremediation and biosensors resulting in pollution control and remediation of environmental media;

(b) Synthesizing products such as chemicals or drug precursors that are currently extracted from plant or animal sources, thereby reducing the pressure on wild species that are currently threatened due to over harvesting or hunting;

(c) Developing organisms designed to generate biofuels which may lead to decreased dependence on non-renewable energy sources;

(d) In building on the achievements of modern biotechnology in producing agricultural crops that are tolerant to abiotic stress and pests, synthetic biology techniques that are more bioinformatics and computer assisted may potentially have the capability to further refine expression and environmental persistence of the products in the organism;

(e) Restoring genetic diversity through reintroducing extinct alleles, or even "de-extinction" of species.

12. **Organisms and products of synthetic biology could also have some negative impacts on the conservation and sustainable use of biodiversity** including, for example:

(a) Microbes that are intended for release into the environment could have adverse effects due to their potential for survival, persistence and transfer of genetic material to other micro-organisms;

(b) Potential undesired consequences could result from the use of "gene drive" systems to spread traits aimed at the suppression or extirpation of populations of disease vectors (e.g. mosquitoes). One such undesired consequence could be the introduction of new diseases through the replacement of the population of the original disease vector by another vector species ("niche substitution);

(c) Possible toxic and other negative effects on non-target organisms such as soil micro-organisms, beneficial insects, other animals and plants;

(d) Potential negative impacts to the conservation and sustainable use of biodiversity could arise from the transfer of genetic material to wild populations via vertical gene transfer and introgression.

13. **Synthetic biology applications could also have indirect negative impacts on the conservation and sustainable use of biodiversity arising from a large-scale increase in the utilization of biomass.** Much of the synthetic biology research is focused on designing organisms that will use biomass as feedstock to produce fuels, chemicals, and pharmaceuticals. Some applications, e.g. fuel production, would require high amounts of biomass, which could lead to a rapid decline in soil fertility and structure, and contribute to biodiversity loss and climate change through direct and indirect land-use change.

14. **The level of exposure of the environment to organisms and products of synthetic biology will determine the level of biosafety related concerns.** In order to mitigate some of the potential negative impacts on the conservation and sustainable use of biodiversity posed by organisms developed through synthetic biology, containment strategies can be used during their handling. Most of the current and near-term applications of synthetic biology involve living organisms that are intended for contained use in research laboratories and industrial settings. Limited biosafety concerns have been raised for organisms being kept under strict containment conditions and focus on ensuring that appropriate measures are in place to prevent contact with the external environment through unintentional or unauthorized releases. Where applicable, organisms produced through synthetic biology may also be placed under contained use outside of laboratories and industrial facilities by using physical measures to limit their exposure to the environment. However, there is no consensus regarding the degree of physical containment that is needed for organisms developed through synthetic biology. Another emerging strategy is the use synthetic biology techniques to develop organisms that have integrated biocontainment traits as in-built biosafety measures. This can include, for example, the use of trophic containment, introduction of suicide genes or xenobiology, i.e. the use of nucleic acids that contain components that are not found in nature and, therefore, should not hybridize with naturally occurring organisms. There is, however, debate on the efficacy of any biocontainment strategy and whether such systems will ever be fully functional or fail proof.

15. **Applications where the organisms that have been produced using synthetic biology techniques and are intended for environmental release will likely raise different biosafety concerns than those of organisms intended for contained use.** Organisms produced through synthetic biology and introduced into the environment may have adverse effects on the conservation and sustainable use of biodiversity. This includes the potential for invasiveness of the organism which may lead to an adverse effect on native species through the destruction of habitat or a disruption of the trophic cascade. Genes from organisms developed through synthetic biology techniques could also transfer to unrelated species through horizontal or vertical gene transfer which may lead to a loss of genetic diversity and an unintended spread of phenotypic traits. Other unintentional adverse effects may occur and must be assessed on a case-by-case basis. Current provisions and procedures established under the Cartagena Protocol on Biosafety, at the international level, and in many existing national biosafety legislations, at the national level, can effectively cover these areas of biosafety concerns.

16. **Existing biosafety risk assessment frameworks are likely to be sufficient to assess the risks of current and near-term applications of synthetic biology on the conservation and sustainable use of biodiversity. As synthetic biology develops, this assessment may need to be revisited.** Most existing biosafety regulations, including the Cartagena Protocol on Biosafety, rely on case-by-case assessments of risks which take into account the environment which will be exposed to the organism, the characteristics of the organism and its intended uses. Current and near-term commercial applications of synthetic biology build on techniques of modern biotechnology to create organisms with novel combinations of genetic material. As such, the general risk assessment methodology for living modified organisms is expected to be applicable to organisms produced through synthetic biology, albeit specific consideration will likely be needed to identify any gaps that exist in the risk assessment methodologies that are currently in place for living modified organisms and propose guidance on how to fill such gaps. If and when future commercial applications of synthetic biology evolve to use techniques that do not rely on the *in vitro* manipulation of nucleic acids to cause inheritable changes in an organism, current risk assessment methodologies for living modified organisms may no longer be suitable. Some researchers reflect 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.

17. **Synthetic biology could cause major economic shifts with positive and negative consequences.** 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 an economic paradigm shift towards economies in which biotechnology, or industries based on the use of biological resources, contribute a much more significant share. However, how developing countries would fare in such a global "bioeconomy" is not self-evident. As seen with other technologies, it is possible that synthetic biology applications would contribute to economic growth if adopted as niche technologies by developing economies. Moreover, synthetic biology could benefit the economies of developing countries through specific applications where 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 would reinforce inequitable trends in international trade; that the scale of extraction and use of biomass to provide for a global bioeconomy could be ecologically unsustainable; and that natural products currently grown or harvested would be displaced by industrial production from micro-organisms resulting from synthetic biology techniques. The shape of new bioeconomies and their social, economic and cultural impacts will likely be influenced by government policies and regulations.

18. **From a health and social perspective, synthetic biology may bring benefits but also unintended effects.** In relation to human health, further developments in synthetic biology could lead to positive impacts by helping to understand disease mechanisms and through the discovery of new drugs, development of vaccines, gene therapies and diagnostic tools. As is historically the case in human health research, unintentional negative effects from drugs and therapies resulting from synthetic biology techniques may trigger unanticipated adverse effects on human health. Synthetic biology techniques may provide tools to better detect and identify pathogenic agents and responding to biosecurity threats. On the other hand, the components, organisms or products of synthetic biology used in research may also be used for damaging results, such as creating biological weapons or pathogens that target natural resources. In addition to the potential negative environmental impacts mentioned in

paragraphs 12 and 13 above, there is also concern around the social impacts of increased biomass use for the production of fuels, chemicals and pharmaceuticals by organisms engineered through synthetic biology. For example, an increase in the demand for biomass could cause communities to lose access to local natural resources and small-scale subsistence farming to be replaced by large-scale commercial farming practices.

19. **Like other modern biotechnologies, synthetic biology raises ethical questions around the level of predictability of its positive and negative impacts, and how to weigh anticipated impacts and the possibility of unexpected impacts.** Ethicists debate whether the threshold between the modification of existing organisms and the creation of *de novo* organisms has been crossed, and what the ethical implications of this might be. There are also concerns surrounding the effect of synthetic biology on the public perception of biodiversity and conservation. For example, one of the specific applications of synthetic biology are "de-extinction" projects which 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.

20. **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 techniques, components, organisms and products seem to be forming: a system with heavy reliance on patenting the components, organisms and products of synthetic biology, and a system based on a combination of patenting the end organisms and products of synthetic biology while sharing the use of the components (e.g. DNA sequences, methods, software) used in the development of such organisms and products. Depending on the intellectual property rights regime that is mostly applied, innovation in synthetic biology may be encouraged, stifled, or directed towards certain kinds of applications or users.

III. 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

A. Overview

21. **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 the term synthetic biology became widely used 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/or 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.

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

22. **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 for 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.

23. **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.

24. **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 impact 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.

25. **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 preamble of the Convention on Biological Diversity includes the following paragraph: "Noting also that where there is a threat of significant reduction or loss of biological diversity, lack of full scientific certainty should not be used as a reason for postponing measures to avoid or minimize such a threat". 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.

26. **Living organisms resulting from current synthetic biology techniques are "living modified organisms resulting from biotechnololgy" as defined by the Convention on Biological Diversity and 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 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 living modified organisms 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, as far as possible and as appropriate, 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.

27. **Living organisms resulting from current synthetic biology techniques fall under the definition of "living modified organisms" under the Cartagena Protocol for Biosafety. Therefore, the requirements of the Cartagena Protocol pertaining to the transboundary movement, transit, handling and use of 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, also apply.** Currently, living organisms resulting from synthetic biology techniques fulfil the criteria of (i) possessing a novel combination of genetic material, and (ii) resulting from the use of modern biotechnology and are, therefore, "living modified organisms" as

defined in the Cartagena Protocol on Biosafety. The fulfillment of the above criteria may need to be reassessed if and when future technological advances of synthetic biology lead to the creation of living organisms possessing novel combinations of genetic material, which are heritable and do not result from the use of *in vitro* nucleic acid techniques or cell fusion. Some organisms resulting from synthetic biology techniques may fall under exemptions from the Advanced Informed Agreement provisions for living modified organisms, if they are in transit, intended for contained use or for direct use as food or feed, or for processing. The Cartagena Protocol will not apply to the transboundary movement of living organisms produced through synthetic biology that are pharmaceuticals for humans and addressed by other relevant international agreements or organizations. Although living organisms produced through synthetic biology may present characteristics that are not common to all living modified organisms, Annex III of the Protocol, including general principles, points to consider and methodology for risk assessment are still fully applicable to living organisms produced through synthetic biology and to products thereof, namely, "processed materials that are of living modified organism origin, containing detectable novel combinations of replicable genetic material obtained through the use of modern biotechnology".. To ensure the effective application of the provisions in Annex III, it may be necessary to identify elements of risk assessment methodologies that would be specific or particularly relevant to assessing the risks of living organisms developed through synthetic biology.

28. **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.

29. **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.

30. **Some applications of 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, measures taken by WTO members to address these risks would count as sanitary and phytosanitary measures in the sense of the Agreement on the Application of Sanitary and Phytosanitary Measures of the World Trade Organization (SPS Agreement) and would have to comply with the requirements thereof. Measures that directly or indirectly affect international trade are allowed, as long as they are supported by a risk assessment or taken in accordance with international 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. 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 for all forms of synthetic biology techniques clear how these standards could be applied. The standard setting organizations Codex Alimentarius Commission, World Organisation for Animal Health or International Plant Protection Convention have not explicitly addressed synthetic biology.

C. 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

31. **In the cases where synthetic biology utilizes genetic resources and requires access to those resources, applicable access requirements (prior informed consent and mutually agreed terms) would apply in accordance with domestic legislation or regulatory requirements on access and benefit-sharing.** Components used in **s**ynthetic biology include virtual/digital information on functional units of heredity. In this context, it is not clear whether the virtual/digital information about genes and other genetic elements can be considered "genetic resources" or "genetic material" in accordance with the definitions contained in Article 2 of the Convention. It is also unclear to what extent other components used in synthetic biology and the products thereof may be considered "genetic resources" as defined by the Convention.

32. **Synthetic biology applications may be considered as a way of utilizing genetic resources as defined in the Nagoya Protocol.** Synthetic biology also raises a number of questions in relation to the application of the Nagoya Protocol to derivatives. In this regard, it needs to be noted that there are different interpretations regarding how the Nagoya Protocol applies to derivatives. National implementation of the Nagoya Protocol can assist in further clarifying the definition of "utilization" as well as 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 until 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.

33. **The International Treaty on Plant Genetic Resources for Food and Agriculture may be 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 the 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. The functioning and scope of the Multilateral System is currently under review by the Governing Body of the ITPGRFA.

34. **It appears that, in accordance with the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), patents should be available under national law of WTO members (other than LDCs) for innovative products and techniques in the field of synthetic biology, provided that they constitute inventions that comply with the general patentability standards. Select products of synthetic**

biology techniques may fall under the subject matter exclusions 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 prevention of their commercial exploitation is 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 commercialisation of synthetic biology techniques.

35. **The results of current synthetic biology research that is focused on modifying existing "natural" genomes could qualify for the "breeder's right" (a sui generis form of protection for intellectual property rights on plant varieties) under the UPOV Convention.** As far as synthetic biology research may in the future result in the production of entirely novel genomes, it may be able to produce new plant varieties which could be protected by breeder's rights, including varieties that are deemed essentially derived from a protected variety.

D. Gaps in the current regulatory framework

36. **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 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.

37. **Potential gaps may exist with regard to components and products resulting from synthetic biology techniques that are not living modified organisms.** Such gaps could occur where components and products resulting from synthetic biology techniques do not fall within the scope of a treaty regime. For example, components 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.

38. **A number of treaties exist which, in general, provide for mechanisms, procedures or institutions that can address potential negative effects associated with the application of synthetic biology techniques, but where no specific guidance exists for their application.** Even though the requirements of the Cartagena Protocol 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, apply to most, if not all, organisms resulting from current synthetic biology techniques, it may be necessary, for example, to identify elements of risk assessment methodologies that would be specific for living organisms developed through synthetic biology in order to ensure the effective application of the provisions in Annex III to the Cartagena Protocol. As another example, States may be able to establish import restrictions on components, organisms and products resulting from synthetic biology techniques in accordance with the Agreement on the Application of Sanitary and Phytosanitary Measures of the World Trade Organization. However, while specific guidance has been developed for the application of standards to living modified organisms, for example under the International Plant Protection Convention, no such guidance exists for other components, organisms and products resulting from synthetic biology techniques.

39. **In sum, the components, organisms and products resulting from synthetic biology would fall under the scope of a number of regulatory mechanisms.** While some instruments are sufficiently broad to address some of the current issues related to synthetic biology, gaps still exist relating to the practical implementation of these instruments to ensure the conservation and sustainable use of biodiversity, and the fair and equitable sharing of the benefits arising from the utilization of genetic resources. Discussions in

international fora may be needed with a view to addressing the gaps identified in this note in an appropriate, consistent, comprehensive and adaptive manner. This could include a need to consider how to address potential impacts of very low probability but very high magnitude. Further discussions may also be needed if and when the advances in synthetic biology lead to the emergence of new gaps.

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