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SYNTHETIC BIOLOGY
Overview of Activities at the Global, Regional and National Levels

Since 2010, there has been an increasing number discussions by countries on the topic of "synthetic biology", and whether and how it should be defined and regulated. These range from **scientific conferences and workshops, to self-regulation initiatives by the scientific community and industry, to policy developments at the OECD, European Commission, and national governments**. Important outcomes of these activities include:

(i) International Association Synthetic Biology (IASB) 2009: *Code of Conduct for Best Practices in Gene Synthesis*

(ii) United States of America 2010: *New Directions - The Ethics of Synthetic Biology and Emerging Technologies*

Finding: synthetic biology does not present new novel safety or ethical issues that required new regulation or changes to existing regulation.

(iii) United Kingdom 2012: *A Synthetic Biology Roadmap for the UK*

Finding: biosafety risks are covered by existing UK/EU legislation and international conventions for GMOs.

(iv) Three scientific committees of the European Commission 2014-2015: *Opinion on Synthetic Biology – 1: Definition; 2 – Risk assessment methodologies and safety aspects; 3 – Risks to the environment and biodiversity related to synthetic biology and research priorities in the field of synthetic biology*

Finding: genetically modified organisms created by synthetic biology are encompassed by the current regulatory framework (environmental release and contained use) and will remain so in the foreseeable future. Current risk assessment approaches remain applicable.

(v) OECD 2014: *Emerging Policy Issues in Synthetic Biology*

Finding: existing GMO/LMO regulation currently sufficient for synthetic biology.

At the United Nations, the primary forum deliberating the regulation of synthetic biology is the **Convention on Biological Diversity (CBD)** (see Annex 1). The CBD has almost universal ratification among United Nations members (excluding the United States) with 196 parties, and it entered into force in 1993. Synthetic biology emerged in CBD discussions in 2010 in the context of "new and emerging issues relating to the conservation and sustainable use of biodiversity", based on proposals by NGOs. To enable an analysis of Parties' needs and views in this area by the CBD's Subsidiary Body on Scientific, Technical and Technological Issues (SBSTTA), Parties decided at their 11th meeting to request information submissions addressing established "new and emerging issue" criteria. However, SBSTTA-18 concluded that there was insufficient information to make a recommendation. Despite this, Parties agreed at their 12th meeting to establish a work program (2015-2016), which was extended to 2017-2018 during their 13th meeting. These programs include information submissions on a range of topics, online discussion series on additional topics, and an *ad hoc* technical expert group (AHTEG) to deliberate the collected information and make recommendations to SBSTTA. To date, SBSTTA has not completed an analysis of whether synthetic

biology is a new and emerging issue, which should be necessary to justify the increasing resources devoted to this topic under the CBD.

The CBD work programmes have discussed topics including: the definition of synthetic biology; scope and adequacy of existing regulatory oversight for living organisms resulting from synthetic biology, components used and non-living products; regulation of genome editing and gene drives; risk assessment and monitoring; access and benefit sharing; and the potential benefits and adverse effects of synthetic biology. The discussions extend into the CBD's subsidiary Protocols:

(i) Cartagena Protocol on Biosafety (Cartagena Protocol)

The Cartagena Protocol has 171 Parties and it entered into force in 2003. It elaborates rules and procedures for the safe handling, transfer and use of living modified organisms (LMOs) resulting from biotechnology. Issues arising in the CBD synthetic biology work program that overlap with the scope of the Cartagena Protocol include: scope of LMO and "modern biotechnology" definitions, risk assessment and risk management, socio-economic considerations, contained use, detection and identification. The issue of risk assessment has also been deliberated by that work program under the Cartagena Protocol (2015). Liability and redress is also an issue, which is in the scope of the Nagoya-Kuala Lumpur Supplementary Protocol (not yet in force).

(ii) Nagoya Protocol on Access and Benefit Sharing (Nagoya Protocol)

The Nagoya Protocol has 100 Parties (to date) and entered force 2014. It is concerned with the fair and equitable sharing of benefits where genetic resources are utilised. The primary issue arising in the CBD synthetic biology work program that overlap with the scope of the Nagoya Protocol is access and benefit sharing in relation to digital sequence information on genetic resources, with a new work program established on that topic jointly under the CBD and Nagoya Protocol (2017-2018).

Another international treaty with synthetic biology on its agenda is the **Biological Weapons Convention** (BWC), which has 173 parties and entered into force in 1975. The BWC prohibits the synthesis of microbial agents for hostile purposes. Biotechnological developments have long been monitored under the BWC due to its dual-use potential, with the topic of "synthetic biology" arising as early as 2006. Activities on this subject under the BWC consist primarily of monitoring trends (e.g. investment, lowering of technological boundaries) and technological developments, including potential weapon applications and potential beneficial applications. The BWC has not made decisions about the regulation of synthetic biology.

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Annex I
SYNTHETIC BIOLOGY
International Negotiations under the Convention on Biological Diversity
And Their Potential Impact on Research, Development and Use of Synthetic Biology

Background:
What "synthetic biology" is, whether and how it should be regulated, and its potential benefits and adverse impacts are fiercely debated issues under the United Nations Convention on Biological Diversity (CBD). The CBD, and its subsidiary Protocols, are international treaties that elaborate rules and procedures for the safe handling, transfer and use of living modified organisms (LMOs) resulting from biotechnology (Cartagena Protocol); liability and redress for damage to biodiversity resulting from LMOs (Nagoya-Kuala Lumpur Supplementary Protocol); and the fair and equitable sharing of benefits where genetic resources are utilised (Nagoya Protocol). They impact on the regulation of products of modern biotechnology, and therefore synthetic biology, from research activities to the commercialisation of products. The CBD has almost universal ratification among United Nations members (excluding the United States) and is the primary forum for international negotiations on the regulation of synthetic biology.

During the last meeting of the Parties to the CBD (COP-13), held in December 2016, the 196 countries that are CBD Parties established a work programme biased toward creation of a new international regulatory framework for synthetic biology. The debate on this topic under the CBD is very polarized. A number of Parties, supported by NGOs, have a clear mandate opposed to synthetic biology that they are pursuing which calls for a broad definition of synthetic biology that includes the spectrum of "new" and "old" biotechnical tools and techniques, strict application of the precautionary approach in synthetic biology risk assessment, the development of new risk assessment and detection guidance, and a decision leading to the development of a new international regulatory framework that would broadly impact on any biotechnological activities. On the other hand, a number of Parties, supported by the scientific community and companies involved in synthetic biology research and development, hold the view there is no need for Parties to the CBD to develop a new regulatory framework as existing regulatory mechanisms are sufficient for current and foreseeable biotechnological applications. These Parties are of the view that living organisms already developed, or currently under research and development, through techniques labelled as synthetic biology are within the scope of the Cartagena Protocol, including its principles and methodologies of risk assessment.

Primary Issues:
There is strong Party support within the CBD synthetic biology work program for the view that there is no need to develop a new regulatory framework for synthetic biology, or any other rules, procedures or guidance in the absence of demonstrated need. This viewpoint is based on, and supported by, the scientific and regulatory opinions issued by a number of national and international organisations and scientific institutions. However, the Parties and NGOs that are calling for development of additional regulatory oversight for synthetic biology continue to strongly push their viewpoint, despite its lack of credible support. The issues arising in the CBD synthetic biology work program will be discussed at two intersessional meetings prior to the 14th meeting of the Parties to the CBD in November 2018; firstly, at the AHTEG on synthetic biology in Montreal, Canada on 4-8 December 2017; and secondly, with further follow-up negotiations taking place at the 22nd meeting of the CBD's Subsidiary Body on Scientific, Technical and Technological Issues (SBSTTA) in July 2018. The primary issues that will be negotiated at these meetings are outlined as follows:

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1. **<u>Existing Regulatory Oversight Is Sufficient for Current Products Resulting from Synthetic Biology and Falling Under the Scope of the Cartagena Protocol:</u>**
    - Living organisms created through synthetic biology applications and possessing "a novel combination of genetic material obtained through the use of modern biotechnology" are LMOs as defined by the Cartagena Protocol. Components and non-living products of synthetic biology are not in the scope of the Cartagena Protocol; however, they are regulated (where appropriate) by a variety of international and national mechanisms (e.g. chemicals and pharmaceuticals are regulated, as appropriate, by long-established sectorial regulatory regimes governing their safe use and trade).
    - Experts and experienced regulators have not identified specific examples of current and foreseeable synthetic biology applications or resulting organisms in the various information gathering activities under the CBD and Cartagena Protocol that present novel regulatory challenges or biosafety risks that cannot be managed by the existing LMO/GMO regulatory frameworks and approaches to risk assessment and risk management.
    - For these reasons, there is no need to develop new or additional regulatory rules, procedures or guidance for technologies labelled as synthetic biology or their resulting products under the CBD.

2. **<u>It is Not Possible to Define 'Synthetic Biology' In a Way That Is Meaningful and Future-proof for the Range of Potential Applications, Products and Sectors.</u>**
    - Synthetic biology is part of the part of the continuum of development of modern biotechnology spanning more than four decades. Synthetic biology is not a new scientific field or paradigm, rather it is an umbrella term encompassing accumulated and constantly advancing knowledge and understanding in biological engineering. The term is used to represent a heterogeneous mix of activities spanning new and established (and re-labelled) biotechnological methods.
    - Due to the range of sectors, applications and types of products possible with synthetic biology, there is no international consensus on a meaningful, broadly applicable, and future-proof definition, nor is this likely to ever be achieved. This is reflected in the information gathering activities under the CBD and Cartagena Protocol, where Parties have failed to identify or agree on specific current or foreseeable examples of synthetic biology, differentiate synthetic biology from "modern biotechnology" (as defined in the Cartagena Protocol), or identify living products of synthetic biology that were not "living modified organisms" (as defined in the Cartagena Protocol).
    - A definition of synthetic biology is not necessary to conduct scientifically robust assessments of the products and organisms resulting from biotechnology. There is a substantial body of knowledge, experience and expertise with the regulation of biotechnology developed over the past four decades that is directly relevant to the consideration of the potential environmental impacts of the products of synthetic biology. This includes the existing case-by-case approaches to risk assessment and risk management.
    - The synthetic biology discussions under the CBD have been complicated by listing of specific techniques (e.g. genome editing), for which there is no consensus, apparently on the basis of their emergence after the development of the Cartagena Protocol. Genome editing is an enabling technology that should not be confused with synthetic biology, or singled out as characteristic of synthetic biology.

3. **Synthetic biology is not a "new and emerging issues relating to the conservation and sustainable use of biodiversity".**
    - Parties to the CBD have never proposed nor agreed that synthetic biology is a "new and emerging issue" as required under CBD rules of procedure. Despite this, synthetic biology information gathering activities under the CBD have steadily increased since 2010 (e.g. information submissions, online forums, and the AHTEG on Synthetic Biology). The topics of these activities are also repetitive across (CBD vs. Cartagena Protocol) and between (CBD 2015-2016 vs. 2017-2018) work programs, as the same or similar topics are seemingly investigated until a different result is achieved. SBSTTA, the body tasked with clarifying the issue, has not completed this analysis or recommended that synthetic biology is a "new and emerging issue" to the Parties.

Suggested Path Forward:

Due to the lack of examples of challenges to current regulatory frameworks, there is no justification to continue with the development of a program of work on synthetic biology under the CBD. The most appropriate course of action for Parties to the CBD on synthetic biology is ongoing monitoring of biotechnological developments in order to identify such examples if they arise. This work must be based on evidence, and a scope of what is current and foreseeable, and not conceptual research, theories, unrealistic hypotheses, or misleading information.