EMBASSY OF THE REPUBLIC OF THE PHILIPPINES
AMBASSADE DE LA RÉPUBLIQUE DES PHILIPPINES
OTTAWA, CANADA

CN: L-88-2015

30 April 2015

Excellency:

I am pleased to convey and endorse to you that pursuant to the request for submission on synthetic biology per Notification 2015-03 from the Secretariat, the enclosed comments and inputs as requested, coming from Dr. Saturnina Halos, Chair of the Biotechnology Advisory Team of the Department Agriculture.

Please accept the assurances of my highest regard and consideration.

With my good wishes.

Sincerely yours,

PETRONILA P. GARCIA
Ambassador

The Honourable
BRAULIO FERREIRA DE SOUZA DIAS
Executive Secretary
Secretariat of the Convention on Biological Diversity
United Nations Environment Programme
Montreal, Canada

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CBD Synthetic biology

Comments: SATURNINA C. HALOS

1. Information relevant to the work of the AHTEG
   i. How to address the relationship between synthetic biology and biological diversity

   a. Examine the role of biological diversity in advancing synthetic biology work

   b. Distinguishing the various products of synthetic biology as they relate to biological diversity

   c. Examine the possible living, self-reproducing products of synthetic biology that may be released to the environment and their possible effect on biological diversity

   ii. The similarities and differences between components and products of synthetic biology and modern biotechnology as defined by the Cartagena Protocol on Biosafety

   a. The generation of useful living self- reproducing products (living modified organisms - LMOs) through synthetic biology and modern biotechnology is similar – by transferring and expressing useful genes to recipient cells and species

   b. The genes and DNA transferred to a species and the recipient cells differ. In synthetic biology, the transferred gene and DNA are not found in nature and is mostly synthesized in the laboratory or the functional sequence composed of DNA from different sources -natural or synthetic. In modern biotechnology, the transferred gene and DNA is similar to those found in nature.

   iii. Adequacy of national/international instruments to regulate synthetic biology in relation to biological diversity – The current Cartagena Protocol on Biosafety (CPB) and Philippine regulatory policy on modern biotechnology are adequate. However, a review of the risk instruments used by each Party is necessary to ensure that risk raised by products of synthetic biology are adequately addressed.

   iv. Operational definition of synthetic biology - Synthetic biology designs non-living and living useful products using newly designed synthetic or naturally derived DNA and non-DNA molecules in novel configurations and are not found in nature.

   v. Potential benefits and risks of LMOs derived through synthetic biology - Potential benefits and risks of LMOs derived through synthetic biology is expected to be similar to those derived through modern biotechnology. However, a review of properties of existing and possible products derived through synthetic biology should be done by the AHTEG.

RESPONSE TO INVITATION FOR INPUTS TO NOTIFICATION NO. 2015-013 FROM THE SECRETARIAT OF THE CONVENTION ON BIOLOGICAL DIVERSITY (CBD) ON THE SUBMISSION OF INFORMATION ON SYNTHETIC BIOLOGY, WITH ATTACHED DECISION X11/24 OF THE CBD CONFERENCE OF PARTIES

Prepared by

FRANCO G. TEVES
Chair, MSU-IIT IBC

a) Information that is relevant to the work of the Ad Hoc Technical Expert Group (AHTEG) on Synthetic Biology:

i. How to address the relationship between synthetic biology and biological diversity.

There is no doubt that synthetic biology will forcibly contribute to an increase in biological diversity by several factors, if the momentum of current synthetic biology experiments continue to rise at least within a period of time. There may come a point when the classification of products of synthetic biology necessitate the creation of new taxa as the genetic and phenotypic traits of the former may no longer fall within any of the conventional taxonomic boundaries. Since the survival characteristics of products of synthetic biology are predictably more robust than those generated through natural selection or conventional breeding, there is also the possibility of eventual loss of the naturally selected or conventionally bred species through displacement in their natural habitats as the species compete for space and other resources. This is in addition to possible horizontal transfer of genetic materials to non-synthetic bioresources. These possibilities need to be addressed in discussions on the potential impact of synthetic biology on biological diversity.

ii. The similarities and differences between living modified organisms (as defined in the Cartagena Protocol) and organisms, components and products of synthetic biology techniques.

The undersigned conforms to the general notion that living modified organisms as defined in the Cartagena Protocol have something in common to products of synthetic biology in that they are both generated through genetic manipulation, though in the case of the latter, the degree of manipulation is more expansive using modified techniques in current gene technologies. They may differ in that products of synthetic biology may be novel such as non-conventional proteins built with non-conventional amino acids having new properties never observed before in natural proteins. Some types of products of synthetic biology such as protocells, though may be able to support metabolic processes through genetic and metabolic engineering, are not capable of self-duplication. Similarities may be more on the structural phenotypic level whereas differences will be more on the genotypic and functional phenotypic categories.

iii. Adequacy of existing national, regional and/or international instruments to regulate the organisms, components or products derived from synthetic biology techniques.

At the moment, laws and policies regulating genetically modified organisms based on the Cartagena Protocol may also be applied to regulate products of synthetic biology. However, there may be a need to also expand the scope of such laws and policies to include regulation of products of synthetic biology. Not until we know more adequately the biology of these novel organisms, including their invasiveness, ease of genetic transfer, extent of pathogenicity, life cycle, and survival strategies, among others, such should be treated under the highest containment levels, and in the highest risk group category which should be stipulated in the expanded laws and policies.

iv. An operational definition of synthetic biology, comprising inclusion and exclusion criteria.

It has been observed that most definitions of synthetic biology formulated by various researchers deal mainly with the conceptual aspects (rational design, standardization, modularization, and engineering). The undersigned adheres to the operational definition generally accepted in the European Community as "*the application of science, technology and engineering to facilitate and accelerate the design, manufacture and/or modification of genetic materials in living organisms.*" The differentiating word here is "accelerate" between GMOs and products of synthetic biology.

For the inclusion criteria for synthetic biology, any process that accelerates genetic modification and increases its predictability using available recombinant DNA technologies would fall under synthetic biology. Those that are not capable of gene transmission, or self-replication, such as "protocells" are excluded from synthetic biology. It would be prudent to add quantifiable parameters for a clearer differentiation between genetic modification based on the Cartagena Protocol and the new synthetic biology. These parameters could include the length of time by which genetic modification is completed, the degree of genetic modification based on number of independent modifications and complexity of such modifications compared to conventional genetic modification, and the novelty of computational methods used.

v. Potential benefits and risks of organisms, components and products arising from synthetic biology techniques to the conservation and sustainable use of biodiversity and related human health and socioeconomic impacts relevant to the mandate of the Convention and its Protocols.

Synthetic biology could generate new types of proteins never seen before in the natural world with the inclusion of non-conventional amino acid residues. Such novel proteins may exhibit new biological activities which may find application in medicine such as in cancer therapy, treatment of multiple drug resistant infectious agents; in agriculture, for GM crops that combine desirable species-specific traits providing complete arrays of essential amino acids, micronutrients, health-promoting fatty acids, and polysaccharides all in one new synthetic biological crop. Cultivation of such novel crops can lessen the demand for the harvesting of several types of conventional crops as well as bioresources that are scarce, promoting conservation and sustainable use of biodiversity. These may also promote natural healing processes reducing dependence on drugs and disease incidence, and therefore, also reducing cost for medical care. Synthetic

biology can also perfectly fit into the practice of precision agriculture. Predictably, the potential for novel applications of products of synthetic biology in nanobiotechnology is high.

While the potential advantages of synthetic biology may be almost limitless, yet because it is still difficult to have a fairly reliable prediction of long-term outcomes and impacts on human health, environmental sustainability, conservation of biodiversity, and effectiveness of state-of-the-art control measures, it may be prudent to consider as well the number and degree of potential harm emanating from synthetic biology researches. Gene flow from organisms which are products of synthetic biology to wild type forms, potential robust invasive traits displacing native species disrupting the biodiversity balance, pathogens acquiring more virulent traits against which herd immunity may be non-existent endangering human and animal populations. In this scenario, burden on human and animal health and environmental mitigation may offset any economic gain. Moreover, the survival of indigenous peoples dependent on native plant and animal species for generations may be put at risk with the appearance of new invasive species overwhelming and replacing the former.

vi. Best practices on risk assessment and monitoring regimes currently used by Parties to the Convention and other Governments, including transboundary movement, to inform those who do not have national risk assessment or monitoring r reseaegimes, or are in the process of reviewing their current risk assessment or monitoring regimes.

Risk assessment is probably one of the most elusive areas of concern in synthetic biology. Based on available information, risk assessment protocols for synthetic biology are still in discussion stages. One of the most defined discussions are those emanating from the joint project of three European Scientific Committees: Scientific Committee on Health and Environmental Risks (SHCER), Scientific Committee on emerging and Newly Identified Health Risks (SCENIHR), and Scientific Committee on Consumer Safety (SCCS).

Points for discussion include the following:

- Implications for human and non-human animal health and the environment of likely developments in Synthetic Biology resulting or not in a genetically modified organism
- Appropriateness of existing methodologies to assess the potential risks associated with different kinds of activities, tools, products and applications arising from Synthetic Biology research
- Adaptation and completion of existing methodologies that are not appropriate to assess potential risks associated with activities related to and products arising from Synthetic Biology research
- Procedure, timing, and extent of inherently building safety locks into products of Synthetic Biology

This is a good example of a consortium effort where experts from several institutions and countries come together and share knowledge and experiences on risk assessment of new-to-nature (NTN) experiments. A similar formal

aggregate of countries and institutions can be formed based on geographical proximity which shall draw the blue print of a general procedure or strategy for designing inherently safe applications of synthetic biology.

Research priorities of the three European scientific committees which may be replicated by similar consortia comprise the following:

- Review the state of the scientific knowledge concerning specific risks to the environment and synthesize it following the procedure and the requirements in the Decision XI/11 of the Convention of Biodiversity including the synthesis of its opinion.
- Identification of the major gaps in knowledge necessary for performing reliable risk assessment in areas of concern
- Recommend proposals on the identified major gaps including methodological guidance on the experimental design and on the requirements of the proposals, to ensure data quality and comparability, and usability of results for risk assessment.

Countries which still do not have formal national risk assessment or monitoring programs can be part of a consortium with countries which do have. With this set up, transboundary arrangements can be easily agreed upon.

vii. The degree to which the existing arrangements constitute a comprehensive framework in order to address impacts of organisms, components and products resulting from synthetic biology relevant to the objectives of the convention on Biological Diversity and its Protocols, in particular threats of significant reduction or loss of biological diversity.

Comprehensiveness of any framework agreed upon by members of consortia for addressing impacts and threats leading to significant reduction or loss of biodiversity can be achieved using the following pillar discussion questions based on the SYNBIOSAFE project of the European Community:

- How should research institutions and industry be regulated to prevent misuse and accidents without hindering development in synthetic biology?
- How should commercial DNA synthesis companies ensure that orders requested by their clients are not used to produce dangerous pathogens?
- What happens when a technology that can greatly benefit society also has military applications?
- How do we balance biosafety with academic freedom?
- How will people respond to the potential of synthetic biology and will they recognize its benefits?
- Are there ethical boundaries that the public will accept or impose, and will these boundaries change over time?

Debates, e-fora, media briefings, national and international workshops should be encouraged at an early stage.

b) Information on measures undertaken in accordance with paragraph 3 of the decision, including the identification of needs for guidance.

Considering that discussions on synthetic biology have just been initiated in the Philippines, it is recommended that all the information stated in section a) of this response be considered section. COP X1/11 on *New and Emerging Issues Relating to the Conservation and Sustainable Use of Biodiversity* paragraph 3 is amply answered in the preceding items.

c) Further information on the 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.

A few specific examples of synthetic biology projects mentioned in the report of the three Scientific Committees of the European Community can be very good case studies for inter-institution, inter-country discussions:

1. BIOMODULARH2: Engineered Modular Bacterial Photoproduction of Hydrogen

   The objectives of this project are the following:

   a. To design reusable, standardized molecular building blocks that would produce a photosynthetic bacterium containing engineered pathways for competitive, clean, and sustainable hydrogen production;
   b. To establish a hierarchical engineering methodology (parts, devises and systems);
   c. To design artificial bacterial systems using a truly interdisciplinary approach that decouples design from fabrication;
   d. To construct biological molecular parts by engineering proteins with new enzymatic activities and molecular recognition patterns, by combining computational and *in vitro* evolution methodologies;
   e. To create an anaerobic environment within the cell for an optimized, highly active, iron-only hydrogenase by using an oxygen-consuming device, connected to an oxygen sensing devise and regulated by artificial circuits.

   Issues that could emanate from this project would include safety in storage of generated hydrogen which is highly combustible; accumulation, storage, and disposal of wastes from such a system; escape of biosynthetic bacterial cells to the environment with an uncertain outcome of interaction with the natural microbiota; energy requirement to sustain such a system on an industrial scale; behaviour of engineered proteins which may be highly stable, with high potential for incorporation in natural cells, and which may have prion-like properties; level of containment for such engineered cells; biosecurity issues including dual military applications.

2. Biology SYNPLEXITY: Dynamic and complexity in synthetic protein networks

The objectives of this project are the following:

a. To implement synthetic protein network motifs (feedback loops, toggle switches) operating in human cell lines;
b. To design swappable interfaces that enable the exchange and rewiring of the different components;
c. To produce raw building blocks derived from modular proteins that transduct signals via auto-inhibition or spatial proximity between individual domains.

Issues that may be of interest in this kind of experiment will be mainly on ethics since the application presumably is on humans.

3. CELLCOMPUT: Synthetic protein networks, Biological computation built on cell communication systems

The major objective of this project is to develop new approaches to cell communication systems that generate building blocks for biological computation devices.

Issues emanating from this project include ethics since the expected product are designed cells that would detect diseased tissues in the human body and produce the compounds necessary to treat the sickness. In addition, the possibility of such designed cells for dual use for delivering toxins or poisons, or becoming weaponized, is a biosecurity issue.

United Nations Decade on Biodiversity

Ref.: SCBD/BS/CG/MPM/DA/84279

6 February 2015

NOTIFICATION

Submission of Information on Synthetic Biology
(action required by 30 April 2015)

Dear Madam/Sir,

In decision XII/24, the Conference of the Parties established an Ad Hoc Technical Expert Group (AHTEG) on Synthetic Biology with terms of reference contained in the annex to the decision, and requested the Executive Secretary to convene a moderated open-ended online forum to support the work of the AHTEG. Decision XII/24 is annexed hereto for ease of reference.

In that same decision, the Conference of the Parties invited Parties, other Governments, relevant international organizations, indigenous and local communities and other relevant stakeholders to submit to the Executive Secretary:

(a) Information that is relevant to the work of the AHTEG, including views on:

(i) How to address the relationship between synthetic biology and biological diversity;

(ii) The similarities and differences between living modified organisms (as defined in the Cartagena Protocol) and organisms, components and products of synthetic biology techniques;

(iii) Adequacy of existing national, regional and/or international instruments to regulate the organisms, components or products derived from synthetic biology techniques;

(iv) An operational definition of synthetic biology, comprising inclusion and exclusion criteria;

(v) Potential benefits and risks of organisms, components and products arising from synthetic biology techniques to the conservation and sustainable use of biodiversity and related human health and socioeconomic impacts relevant to the mandate of the Convention and its Protocols;

(vi) Best practices on risk assessment and monitoring regimes currently used by Parties to the Convention and other Governments, including transboundary movement, to inform those who do not have national risk assessment or monitoring regimes, or are in the process of reviewing their current risk assessment or monitoring regimes;

(vii) The degree to which the existing arrangements constitute a comprehensive framework in order to address impacts of organisms, components and products resulting from

To: CBD National Focal Points; relevant organizations; and indigenous peoples and local communities

cc: SBSTTA National Focal Points, Cartagena Protocol National Focal Points, Nagoya Protocol Focal Points

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synthetic biology relevant to the objectives of the Convention on Biological Diversity and its Protocols, in particular threats of significant reduction or loss of biological diversity;

(b) Information on measures undertaken in accordance with paragraph 3 of the decision, including the identification of needs for guidance; and

(c) Further information on the 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.

Accordingly, I would kindly invite you to submit to the Secretariat (secretariat@cbd.int) any currently available information on the aforementioned topics as soon as possible, but no later than **30 April 2015**. The information submitted will serve as a basis for the deliberations of the online forum and the AHTEG on synthetic biology.

A separate notification outlining the activities of the online forum and AHTEG, including the procedure for the nomination of participants, which is envisaged to start on 1 March 2015, will be sent out by the Secretariat in due course. A tentative calendar of activities in this process is available at https://bch.cbd.int/calendar_synbio.shtml.

Please accept, Madam/Sir, the assurances of my highest consideration.

Braulio Ferreira de Souza Dias
Executive Secretary

Annex

DECISION ADOPTED BY THE CONFERENCE OF THE PARTIES TO THE CONVENTION ON BIOLOGICAL DIVERSITY

XII/24. New and emerging issues: synthetic biology

The Conference of the Parties,

Reaffirming paragraph 4 of decision XI/11, in which it recognized 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,

Noting decision BS-VII/12 of the Conference of the Parties serving as the meeting of the Parties to the Cartagena Protocol on Biosafety, recommending a coordinated approach on the issue of synthetic biology taking into account that the provisions of the Cartagena Protocol may also apply to living organisms resulting from synthetic biology,

1. *Takes note* of the conclusions of the Subsidiary Body on Scientific, Technical and Technological Advice at its eighteenth meeting, as contained in paragraph 1 of recommendation XVIII/7, *recognizes* that this issue is of relevance to the Convention and *concludes* that there is currently insufficient information available to finalize an analysis, using the criteria set out in paragraph 12 of decision IX/29, to decide whether or not this is a new and emerging issue related to conservation and sustainable use of biodiversity;

2. *Awaits* the completion of a robust analysis using the criteria set out in paragraph 12 of decision IX/29;

3. *Urges* Parties and *invites* other Governments to take a precautionary approach, in accordance with paragraph 4 of decision XI/11, and:

(a) To establish, or have in place, effective risk assessment and management procedures and/or regulatory systems to regulate environmental release of any organisms, components or products resulting from synthetic biology techniques, consistent with Article 3 of the Convention;

(b) To approve organisms resulting from synthetic biology techniques for field trials only after appropriate risk assessments have been carried out in accordance with national, regional and/or international frameworks, as appropriate;

(c) To carry out scientific assessments concerning organisms, components and products resulting from synthetic biology techniques with regard to potential effects on the conservation and sustainable use of biodiversity, taking into account risks to human health and addressing, as appropriate, and according to national and/or regional legislation, other issues such as food security and socioeconomic considerations with, where appropriate, the full participation of indigenous and local communities;

(d) To encourage the provision of funding for research into synthetic biology risk assessment methodologies and into the positive and negative impacts of synthetic biology on the conservation and sustainable use of biodiversity, and to promote interdisciplinary research that includes related socioeconomic considerations;

(e) To cooperate in the development and/or strengthening of human resources and institutional capacities, including on methodologies for risk assessments in synthetic biology and its potential impacts on biodiversity, in developing countries, in particular the least developed countries and small island developing States, and countries with economies in transition, including through existing global, regional and national institutions and organizations and, as appropriate, by facilitating civil society involvement.

The needs of developing country Parties, in particular the least developed countries and small island developing States among them, and Parties with economies in transition, for financial resources; access to and transfer of technology consistent with Article 16 of the Convention; establishing or strengthening regulatory frameworks; and the management of risks related to the release of organisms, components and products resulting from synthetic biology techniques, should be taken fully into account in this regard;

4. *Decides*, subject to the availability of resources, to establish an Ad Hoc Technical Expert Group, with terms of reference contained in the annex to the present decision, to be convened after the Executive Secretary has completed the requests in paragraph 7 below;

5. *Invites* Parties, other Governments, relevant organizations and stakeholders to submit information to the Executive Secretary relevant to the work of the Ad Hoc Technical Expert Group established by the present decision, as well as on measures undertaken in accordance with paragraph 3 above, including the identification of needs for guidance;

6. *Invites* Parties, other Governments, relevant international organizations, indigenous and local communities and relevant stakeholders to continue to provide further information to the Executive Secretary in response to decision XI/11, paragraph 3 (a);

7. *Requests* the Executive Secretary, subject to the availability of financial resources:

(a) To make available the information reported in accordance with paragraphs 5 and 6 above, through the clearing-house mechanism of the Convention and other means;

(b) To convene a moderated open-ended online forum[1] to support the work of the Ad Hoc Technical Expert Group established in paragraph 4 above in meeting its terms of reference;

(c) To prepare an updated report on the work specified in paragraphs 3 (a), 3 (b) and 3 (c) of decision XI/11, taking into account information submitted in paragraphs 5 and 6 above and a synthesis of the outcomes of the process mentioned in paragraph 7 (b) and to submit these for consideration by the Ad Hoc Technical Expert Group;

(d) To submit for consideration by a meeting of the Subsidiary Body on Scientific, Technical and Technological Advice prior to the thirteenth meeting of the Conference of the Parties, the peer-reviewed reports of the outcomes of the process mentioned in paragraphs 7 (b) and 7 (c) above;

8. *Invites* relevant organizations, including relevant United Nations organizations and bodies, to consider the possible implications of synthetic biology as it relates to their mandates.

Annex

TERMS OF REFERENCE FOR THE AD HOC TECHNICAL EXPERT GROUP ON SYNTHETIC BIOLOGY

The Ad Hoc Technical Expert Group will include balanced representation of Parties from all regions and include representation of indigenous and local communities and all relevant stakeholders, including other Governments, with knowledge of the Convention and its Protocols,[2] and will report on its work to a meeting of the Subsidiary Body on Scientific, Technical and Technological Advice prior to the thirteenth meeting of the Conference of the Parties.

The Ad Hoc Technical Expert Group will:

(a) Take note of the exchange of views on how to address the relationship between synthetic biology and biological diversity;

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[1] The open-ended online forum will be open to all interested participants and continue for a finite period of time.

[2] The Ad Hoc Technical Expert Group will be convened in accordance with the *modus operandi* of the Subsidiary Body on Scientific, Technical and Technological Advice, except that there will be 5 to 8 experts nominated by each of the five regions.

(b) Identify the similarities and differences between living modified organisms (as defined in the Cartagena Protocol) and organisms, components and products of synthetic biology techniques to determine if living modified organisms derived from synthetic biology fall under the scope of the Cartagena Protocol;

(c) Identify if other national, regional and/or international instruments adequately regulate the organisms, components or products derived from synthetic biology techniques in so far as they impact on the objectives of the Convention and its Protocols;

(d) Work towards an operational definition of synthetic biology, comprising inclusion and exclusion criteria, using all relevant information, based on scientific and peer-reviewed studies;

(e) Identify the potential benefits and risks of organisms, components and products arising from synthetic biology techniques to the conservation and sustainable use of biodiversity and related human health and socioeconomic impacts relevant to the mandate of the Convention and its Protocols;

(f) Building on the work on risk assessment and risk management undertaken by the Cartagena Protocol, compile information on best practices on risk assessment and monitoring regimes currently used by Parties to the Convention and other Governments, including transboundary movement, to inform those who do not have national risk assessment or monitoring regimes, or are in the process of reviewing their current risk assessment or monitoring regimes and to help those Parties and other Governments to regulate organisms, components and products from synthetic biology techniques appropriately;

(g) Identify if the existing arrangements constitute a comprehensive framework in order to address impacts of organisms, components and products resulting from synthetic biology relevant to the objectives of the Convention on Biological Diversity and its Protocols, in particular threats of significant reduction or loss of biological diversity.
