**“Submission of information on synthetic biology and nomination of experts to participate in the Open-ended Online Forum on Synthetic Biology”**

**(a) The relationship between synthetic biology and the criteria set out in decision IX/29, paragraph 12, in order to contribute to the completion of the assessment requested in decision XII/24, paragraph 2, building on the preliminary analysis prepared by the Executive Secretary in document SBSTTA/22/INF/17;**

Regarding this item, it is very important to highlight that it is the first time that the criteria established in the paragraph 12 of Decision IX/29 is being used to analyze a topic to be considered as a New and Emerging Issue (NEI) under the Convention on Biological Diversity (CBD) agenda.

In this regard Brazil considers that a very strict and robust evaluation of those criteria is followed and agreed by consensus, as not to open a precedent for future topics. Any topic included in the CBD agenda demands a lot of extra effort and resources and therefore Brazil considers that the agenda is already very ambitious with the goals of the Aichi Targets to be met and with the building of the post 2020 agenda.

In this sense Brazil would like to highlight again that the criteria in the paragraph 12 of Decision IX/29 were not fulfilled, in particular the items:

(b) New evidence of unexpected and significant impacts on biodiversity;

(c) Urgency of addressing the issue/imminence of the risk caused by the issue to the effective implementation of the Convention as well as the magnitude of actual and potential impact on biodiversity; and

(e) Evidence of the absence or limited availability of tools to limit or mitigate the negative impacts of the identified issue on the conservation and sustainable use of biodiversity;

Brazil considers that there are enough elements available in the peer review publications and also in the Synthetic Biology AHTEG reports (UNEP/CBD/SYNBIO/ AHTEG/2015/1/3 and UNEP/CBD/ SYNBIO/AHTEG/2017/1/3) with the main conclusion that:

*“The AHTEG agreed that living organisms developed through current and near future applications of synthetic biology are similar to LMOs as defined in the Cartagena Protocol”*

Also Brazil notes that the potential adverse effects with respect to conservation of biological diversity listed in the first Ad Hoc Technical Expert Group (AHTEG) report are the same effects considered in the case of LMO risk assessment and it is recognized in the second report:

*“…the AHTEG recalled the conclusion reached at its previous meeting that the organisms, components and products of synthetic biology were expected to have similar types of positive and negative impacts on biological diversity as classical genetic engineering”*

In this case it is possible to conclude that may be challenges in the future developments in the field of Synbio, but to better understand both the positive and negative impacts of Synbio organisms there is already the experience of decades with risk assessment and risk monitoring of Living Modified Organisms (LMOs) as a good basis to face those challenges.

Concluding, there are regulations and tools in place under the Cartagena Protocol on Biosafety (CPB) that allow the monitoring of technology development, a conclusion corroborated by some of the AHTEG report conclusions:

*“Create or expand existing online platforms to facilitate knowledge and information sharing on risk assessment research, positive and negative impacts of synthetic biology through, among other things, the Biosafety-Clearing House or the clearing-house mechanism”.*

*“The AHTEG noted that most tools that were currently in use for the detection, identification and monitoring of LMOs could also be used for organisms developed through synthetic biology, but those tools might need to be updated and adapted”*

*“The AHTEG reiterated that the general principles and methodologies for risk assessment under the Cartagena Protocol and existing national biosafety frameworks, as well as voluntary guidance, could provide a good basis for risk assessment of organisms developed through synthetic biology. These methodologies might need to be periodically updated and adapted"*

*“Current strategies for risk management and monitoring of LMOs might provide a good basis for managing the risks and monitoring potential impacts of organisms developed through synthetic biology. These strategies might need to be adapted and complemented in order to address specific characteristics of organisms developed through synthetic biology”.*

Thus, Brazil would like to thank the Secretariat for the analysis of the reports of the first and second meetings of the Synbio AHTEG in the Document SBSTTA/22/INF/17 and also for providing possible answers for the criteria set out at Decision IX/29, Paragraph 12.

However, considering:

a) the procedural rite established in the CBD to elect a subject like New and Emerging Issue (NEI);

b) following the same Decision IX/29, Paragraph 12;

c) the Decision XII/24, Paragraph 2;

d) the Term of Reference (TOR) of the AHTEG of Synbio;

e) the consideration of AHTEG members that agreed to defer the analysis requested of these criteria until further guidance on how to apply the criteria for the selection of on the NEI was provided by the Conference of the Parties (COP); and

f) that the Recommendation XI/7 of the SBSTTA 21 did not provide a guidance,

Brazil considers that the criteria for Synbio to be considered a NEI have not yet been completed and that this analysis must be performed by the Synbio AHTEG, as previously defined by the Parties in its TOR. Additionally Brazil requests that the guidance on how to apply the criteria for the selection on the NEI be provided by Parties at the COP15.

**(b) New technological developments in synthetic biology since the last meeting of the Ad Hoc Technical Expert Group in December 2017, including the consideration, among other things, of concrete applications of genome editing if they relate to synthetic biology, in order to support a broad and regular horizon scanning process;**

According to the definition of Synthetic Biology (Synbio) on the CBD Decision XIII/17, paragraph 4, all kind of technological development using genome-editing systems based on news biotechnology tools - for example: CRISPR, Transcriptional Activator-Like Effectors Nucleases (TALENS) and Zinc-Finger nucleases (ZFNs) - are considered examples of the use of Synbio. Thus, any new technological developments made using these tools in organisms are examples or concrete applications of the genome editing related to Synbio.

Since the last Synbio AHTEG meeting there have been several examples of concrete applications using the new tools of genic editing highlighting their importance in different areas, such as biomedical research, drug discovery and development, gene therapy1, control of disease vectors11, etiological agent12 and insect agricultural pests5.

In order to have a dimension of how these tools are important for new technological developments, it is estimated that, in the next decade, it will increase by 200% the identification of the number of genes related to Mendelian diseases and/or those that make the organism more susceptible to diseases and infections, such as cystic fibrosis and Duchenne muscular dystrophy, for example1,2.

Other examples of new technological developments can be verified in Protein therapeutics that use Synbio to produce and treat genetic and regulatory disorders3 through production of biological molecules in different biological systems, or through the correction in the production or regulation of these same biological molecules in the organisms themselves, through gene editing1,3,4.

The development of new Sterile Insect Techniques (SIT) as Precision Guided SIT (pgSIT), which are based on CRISPR, have the potential to provide worldwide solutions to combat vector of important diseases typical of emerging countries that have limited capacity to combat them, such as: malaria, dengue, Zika, and Chikungunya5. The same technological development can be used to improve the fight against several pests that impact agriculture and food production, and the damages on ecosystems and threats to biological diversity caused by invasive species5, 7. Likewise, pgSIT or similar technological developments using Synbio and genome editing technologies can be used to restore habitats, preserve endangered species, and to promote the development of organisms that are more productive or more adapted to climate change in more quickly, accurately and securely ways.

It is important to emphasize that in many countries, particularly in emerging countries, agriculture plays a central role in the economic and social sectors. Thus, new tools that benefit agriculture will benefit all other related areas.

Even for the combat of etiological agents in which other options of treatment have not been proved effective, such as the treatment of AIDS virus infection, the use of Synbio and genome editing may represent a promising alternative of treatment and cure12.

Another approach that has grown considerably through what is considered Synbio and genome editing by CBD is Gene Therapy. An important benefit of this approach is a single treatment that allows achieving durable curative clinical benefits6. Gene-based therapies can promote sustained production of endogenous proteins, such as clotting factors in hemophilia6. Even more promising, recent clinical studies have found that single infusions of T cells engineered with synthetic genes can produce durable responses against tumor cells6, 8. This perspective of treatment using modified gene and cell therapies has the ability to fight virtually all existing forms of cancer.

The potential for gene therapy to provide durable and sustainable benefits to human health using Synbio and genome editing allied to clinical successes over the past several years makes this one of the most promising fields for future health care6.

The “Horizon Scanning Mechanism” already exists under CBD through the Biosafety Clearing-House (BCH), the Subsidiary Body on Scientific, Technical and Technological Advice (SBSTTA), the submissions of information from countries etc. Brazil considers that it is not necessary to duplicate efforts through a specific mechanism as there is already a very ambitious agenda under CBD and that efforts and resources need to be concentrated on existing mechanisms.

About the applications of genome editing, the regulations of each country will establish the applicable conditions. If the organism produced by the genome editing technique does not have a recombinant genetic material it could be considered a conventional organism, while an organism obtained by gene editing with the presence of recombinant genetic material could be considered a LMO and follow the biosafety regulations. The use of gene editing techniques by themselves does not classify an organism as an application of Synbio. It becomes necessary to understand the complexity of the modification and the new organism functions for this classification.

**(c) The current state of knowledge by analysing information, including but not limited to peer-reviewed published literature, on the potential positive and negative environmental impacts, taking into account human health, cultural and socioeconomic impacts, especially with regard to the value of biodiversity to indigenous peoples and local communities, of current and near-future applications of synthetic biology, including those applications that involve organisms containing engineered gene drives, taking into account the traits and species potentially subject to release and the dynamics of their dissemination; and**

The Synbio AHTEG report concluded that most living organisms already developed or currently under research and development through techniques of Synbio, including organisms containing engineered gene drives, fell under the definition of LMOs as per the Cartagena Protocol. And the current examples of use of organisms containing engineered gene drive under research presented in the literature can be considered a LMO.

It should be noted that science is still in the initial phase of research with gene drive and it is necessary more research of scientific value in informing an assessment of the potential positive and negative environmental impacts, but is also necessary to recognize the significant benefits from gene drive for developing countries being devastated by tropical diseases and the importance to incentive the research in this area. The precautionary approach regarding gene drive was already recognized by Parties in previous decisions, it´s crucial also to recognize the importance of research with gene drive taking into consideration the human health as part of the CBD global vision.

Brazil considers that is necessary to promote research in areas such as modelling, establishment of scenarios, experiments performed under contained use and to adapt the experience gained in other areas of risk assessment such as management of pests and invasive alien species, LMOs released in the environment, to explore possible positive and negative impacts of near-future applications of Synbio.

Although there are uncertainties and more research is necessary, it is also part of our conclusion about the potential positive impacts of Synbio that to face future challenges and to meet Aichi Targets and Sustainable Development Goals (SDGs) agenda all countries will need to stay abreast of development. The developing countries need to build capacities for research using Synbio tools seeking for local and regional solutions to improve the quality of life and environment conservation and to better understand the potential impacts.

One of the most promising uses of gene drive technology is the possibility of controlling populations of organisms. Through this approach it is possible to: eradicate invasive species that destroy the biological diversity of a given ecosystem; conserve endangered species; support agriculture by reversing pesticide and herbicide resistance in insects and weeds; control damaging invasive species; to help combat pests that threaten food production; and to modify species that transmit important infectious diseases (notably mosquitoes that transmit malaria, dengue, and zika pathogens) to stop this action9.

Another important issue of gene drive approach is its ability to spread a characteristic of interest. In this way, it is possible to use the same gene drive technique, but with a different strategy, to modify organisms preventing them from transmitting infectious diseases, as demonstrated by the Target Malaria10, and to combat pests (herbivorous and disease-vectoring insects, pathogens and weeds) that attack agriculture11.

Faced with so many benefits of using gene drive technology, scientists and regulators have kept the necessary caution to the subject due to the possibility of off-targets and species eradication. Therefore, ways for better controlling the technique are being developed so that there is greater understanding and control (spatial and temporal) in order to limit undesired consequences13.

Another initiative to help improve the understanding of the gene drives approach is the CBD's proposal to discuss the topic and check the possibility of developing a guideline to gene drive.

**(d) Living organisms developed thus far through new developments in synthetic biology that may fall outside the definition of living modified organisms as per the Cartagena Protocol.**

As widely discussed in the meetings and activities involving this issue in the CBD, and after reviewing the scientific literature, it is possible to state that all organisms developed by Synbio are considered a Living Modified Organism (LMO) as defined in Cartagena Protocol on Biosafety (CPB), Article 3:

*“(g) “Living modified organism” means any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology”*

And there was no concrete example of an aspect that would not be considered under the current risk assessment framework under the Cartagena Protocol or under existing regulations.

The general principles of risk assessment, Annex III of the Cartagena Protocol, include a scientifically sound, transparent and comparative approach, recognizing that the absence of scientific knowledge or consensus does not indicate a certain level of risk. The general principles remain applicable to the risk assessment of LMOs developed through Synbio. The information that will be relevant to answer the risk hypothesis for LMOs developed through synthetic biology will vary in nature and detail from case-by-case.

As recognized in the Synbio AHTEG report:

*“Techniques involving cell-free systems did not result in the development of living organisms. Likewise, to date, protocells that were capable of replicating genetic material did not exist and, as such, were not living organisms. In the future, however, protocells that were capable of transferring or replicating genetic material might be developed and those might be regarded as LMOs."*

Although it is currently possible to build large and more complex molecules and modify, create and modulate biological circuit through Synbio there is still a long way to build an organism that may fall outside the definition of LMO as defined in the CPB. In fact, there is no prospect for obtaining this kind of organism in the short and medium term. In the long term when that happens, and if it does, experts on the subject will be ready to discuss, based on scientific evidences, all the steps and procedures that should be taken in the CBD to keep the three principles of the Convention, if needed.

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