Submission of information on synthetic biology

Within the framework of the Convention on Biological Diversity, the Conference of the Parties takes note of new and emerging issues relating to the conservation and sustainable use of biodiversity. In Decision UNEP/CBD/COP/DEC/XII/24 Parties, other Governments, relevant international organizations, indigenous and local communities and other stakeholders were invited to submit relevant information on components, organisms and products resulting from synthetic biology tools that may have impacts on the conservation and sustainable use of biological diversity and associated social, economic and cultural considerations. EuropaBio welcomes the opportunity to submit information.

EuropaBio questions the adequacy of the approach to define 'synthetic biology' by the process applied in the development of products and organisms. We believe it is impossible to define clear boundaries between genetic engineering and 'synthetic biology' in its broad definition today. The tools that may be used in synthetic biology applications build upon and include those defined as 'modern biotechnology' which are the subject of the international regulatory framework established by the Cartagena Protocol on Biosafety. Due to this overlap, the term 'synthetic biology' can be misleadingly applied to include the use of biotechnological tools generally, and to the products of these tools.

Synthetic biology represents a logical further development of existing molecular biology methods and is associated with a large innovation potential from which both basic research and industrial application can profit[1].

The regulation of organisms and/or products developed using 'synthetic biology' tools should be triggered by the nature and characteristics of the product, as opposed to triggered by the process used to develop such products. This is particularly applicable to 'synthetic biology', given the diverse range of tools employed that defy simple categorization, the diversity of potential products, and the fact that it is the characteristics of the product that determine its safety, not the process by which it is produced. The need, if any, for additional or specific regulation of the products of 'synthetic biology' can only be assessed using such an approach.

At present, synthetic biology is mainly concentrated on fundamental research. Most of the current work in the field of synthetic biology is still at the basic research level. The economic implications of synthetic biology cannot be precisely evaluated at present. Even if synthetic biology is still in its infancy, attractive market potentials have already started to emerge[1].

From today's perspective, the aim of synthetic biology – to synthesise genomes in vitro to create novel organisms do not yet mandate additional requirements for biological safety in laboratories or release (biosafety) and do not incur risks with respect to possible misuse (biosecurity) of this technology other than those arising from genetic engineering. Statutory regulation tailored to synthetic biology is thus currently not necessary[1].

[1] Source: Synthetic Biology Statement, DFG, German Research Foundation, July 2009

While the on-line discussion proposes seven Topics, we submit that the definition is of central importance and should be handled first.

Topic 3
Operational definition of synthetic biology, comprising inclusion and exclusion criteria

There is currently no internationally agreed consensus about a definition of synthetic biology.

The term synthetic biology covers a research and application field that cannot be strictly differentiated from conventional genetic engineering and biotechnological processes. It can therefore be regarded as a further development of these disciplines and their respective objectives[2].

Synthetic biology represents a logical further development of existing molecular biology methods and is associated with a large innovation potential from which both basic research and industrial applications can profit. Because the majority of the application-oriented projects are still at the design stage, basic research should be promoted and included to a greater extent in the planning of future scientific funding programmes[2].

From today's perspective, the aims of synthetic biology – to synthesize genomes in vitro and to create novel organisms do not yet mandate additional requirements for biological safety in laboratories or release (biosafety) and do not incur risks with respect to possible misuse (biosecurity) of this technology other than those arising from genetic engineering. Statutory regulation tailored to synthetic biology is thus currently not necessary[2].

One of the most commonly cited[3] definitions (Royal Academy of Engineering, 2009) is:

> *"Synthetic biology aims to design and engineer biologically based parts, novel devices and systems as well as redesigning existing, natural biological systems."*

In the opinion on "Synthetic Biology – Definition" (Scientific Committees to the European Commission, 2014), the Scientific Committees to the European Commission present synthetic biology as:

> *"the application of science, technology and engineering to facilitate and accelerate the design, manufacture and/or modification of genetic materials in living organisms"*

Synthetic biology is the creation of new biological systems that do not occur in nature, and the design of individual molecules, cells, and organisms that exhibit new properties with the

[2] Source: Synthetic Biology Statement, DFG, German Research Foundation, July 2009

[3] This definition has been quoted e.g. in
- S.R. Carter, Rodemeyer M., Garfinkel M.S., & Friedman R.M. (2014) Synthetic Biology and the U.S. Biotechnology Regulatory System: Challenges and Options. J.Craig Venter Institute.
- UNEP/CBD/COP/12/INF/11 (2014)
- Scientific Committee on Health and Environmental Risks, Scientific Committee on Emerging and Newly Identified Health Risks, and Scientific Committee on Consumer Safety (2014) Opinion on Synthetic Biology I - Definition
- OECD (2014), Emerging Policy Issues in Synthetic Biology, OECD Publishing, Paris. DOI: http://dx.doi.org/10.1787/9789264208421-en

aid of procedures from molecular biology and standardized principles and methods from engineering science[4].

At present, synthetic biology is mainly concentrated on fundamental research. Most of the current work in the field of synthetic biology is still at the basic research level[5].

These two definitions are good examples of definitions of 'synthetic biology' in general and good illustration of the challenge in defining synthetic biology beyond broad lines. However, these definitions underline the notion of technological continuum that is present between existing and more advanced or new approaches in genetic engineering.

The term synthetic biology covers a research and application field that cannot be strictly differentiated from conventional genetic engineering and biotechnological processes. It can therefore be regarded as a further development of these disciplines and their respective objectives. The current work in the field of synthetic biology is still at the basic research level [5]. For the purpose of the CBD discussion, we stress that synthetic biology should go beyond the broad concept of modification of genetic material and organisms. It should be restricted to the bottom-up, de-novo creation of organisms.

Topic 1
How to address the relationship between synthetic biology and biological diversity
Given the vast diversity of potential applications of synthetic biology, ranging from components, to cells and organisms, a transparent pragmatic approach is required. Such an approach should provide clarity to researchers and developers, as well as provide confidence to regulators and society.

EuropaBio proposes that the following guiding principles:

- **Future applications of synthetic biology, in its broadest definition, hold the potential to bring major progress in life science and to deliver to a broad public improved products that are beneficial for the environment and the conservation and sustainable use of biological diversity.**
  Several studies indicate the potential for improving production processes and final products in fields ranging from food and fuel production, responding to climate change, water conservation, and environmental remediation. Any regulatory approach must balance the potential risks against the benefits of such applications - based on sound science.

- **Future applications of synthetic biology properly managed in containment are not expected to present a threat to biological diversity.**
  So far, applications of "synthetic biology" utilize tools associated with conventional biotechnology and concern processes conducted in controlled environments, such as fermenters. In this case, the long-established principles and procedures of biological containment apply, and the potential direct impact on biological diversity will be negligible.

- **The current work in the field of synthetic biology is still at the basic research level. This research uses existing organisms. The scientific information on these organisms will be the basis to understand the relationship with biological diversity.**

[4] Source: Synthetic Biology, TAB-Brief Nr. 39/Special Edition
[5] Source: Synthetic Biology Statement, DFG, German Research Foundation, July 2009

Many applications of 'synthetic biology' will involve engineered components and pathways in organisms (e.g. bacteria, yeast, plants) that are otherwise unchanged. In many cases, the engineered characteristics are unlikely to influence the behaviour or the biology of the recipient organism, and consequently the relationship with biodiversity. Recipient organisms for such applications will be selected based on the available knowledge, the readiness of engineering techniques and their suitability for the intended use. This information can provide a reference for evaluating the relationship with biodiversity.

Topic 2
Similarities and differences between living modified organisms (as defined in the Cartagena Protocol) and organisms, components and products of synthetic biology techniques

Article 3 of the Cartagena Protocol proposes the use of terms for the purpose of the Protocol. The following definitions are of particular relevance to the synthetic biology discussion:

- **"Living organism"** *means*
  any biological entity capable of transferring or replicating genetic material, including sterile organisms, viruses and viroids

- **"Living modified organism"**
  means any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology

- **"Modern biotechnology"**
  means the application of:
  a. In vitro nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles, or
  b. Fusion of cells beyond the taxonomic family,
  that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection.

As pointed out in several reports, applications of 'synthetic biology' use the tools of 'modern biotechnology The organisms used can be unmodified or modified. Modified organisms, if possessing a novel combination of genetic material obtained through the use of modern biotechnology are by definition 'Living Modified Organisms'. The fact that an *in vitro* nucleic acid technique uses a sequence isolated from an organism or a synthetically composed sequence is irrelevant within this definition. In both cases it results in a novel combination of genetic material through the use of modern biotechnology. Even if a 'synthetic biology' approach was used to introduce a novel pathway, introducing this novel pathway in a recipient organism can result in an LMO.

Topic 4
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

EuropaBio appreciate that the fact-finding effort includes looking at potential benefits as well as potential risks. Reports like UNEP/CBD/COP/12/INF/11 and OECD (2014) provide good overviews of potential benefits and risks. It is stressed that synthetic biology is an approach with potential applications in several market sectors, such as energy, chemicals, medicine, environment and agriculture.

As emphasised throughout this submission, the capacity to yield benefits or bring harm can only be assessed by reference to the characteristics of the organism used. Furthermore, the realisation of a benefit or risk is determined by the intended activity and the environment in which this activity will take place. Given the broad potential applications of synthetic biology, an evaluation of potential benefits and risks is possible on a case by case basis. Some cases, such as fermentation processes, can be generally regarded as low risk.

Another area in relation to risks is biosecurity. Biosecurity concerns related to biodiversity include the use of synthetic biology to create destructive pathogens targeting agriculture or other natural resource bases. While this is an important concern, we submit that biosecurity is a general aspect of all life science research and that other frameworks (*e.g.* the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction (Biological Weapons Convention–BWC)) are specifically suited for this.

Topic 5
Best practices on risk assessment and monitoring regimes currently used by Parties to the Convention and other Governments

As most of the alleged synthetic biology applications can also be LMO, EuropaBio submits that they can be handled in a similar way. This is in line with recommendations from e.g.:

- **EU:** Although SynBio is relatively a new field, the existing regulations applicable to biological, chemical or genetic modification research and products are also applicable to SynBio research, applications and products (Annex IV). In particular, the safety and regulatory aspects for SynBio are considered in light of the current EU GMO regulatory framework (embodied by EU Directives 2001/18/EC regulating deliberate release, and 2009/41/EC regulating contained use)[6].

  At the regulatory level, the main conclusion that can be drawn to date is that current activities involving the development and use of synthetic organisms make use of techniques that fall within the scope of Directives 2009/41/EC and 2001/18/EC. In consequence the European GMO regulatory framework is for the moment adequate to support risk assessment of these activities. This applies also to cases where pathogenic micro-organisms are manipulated or reconstituted, since the scope of

[6] Source: SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), SCCS (Scientific Committee on Consumer Safety), SCHER (Scientific Committee on Health and Environmental Risks), Synthetic Biology I Definition, Opinion, 25 September, 2014

the Belgian legislation on contained use of GMOs also covers pathogens. However, it should be noted that some developments of SB (e.g. protocells or orthogonal systems) could raise potential issues as regard the regulatory status of the resulting organisms as these approaches could be considered as not leading to GMO or not meeting the definition of an organism in the meaning of the EU legislation[7].

- **The UK Scientific Advisory Committee on Genetic Modification**
  In the Guidance from the Scientific Advisory Committee on Genetic Modification (update 2007) it is stated:
  > "Containment and control: Given that the goal of synthetic biology is to create novel microorganisms, many of the risks associated with such activities will be complex, indefinable and difficult to anticipate with any degree of precision. Like more traditional GM approaches, however, many of those risks could be estimated based upon knowledge of the microorganisms and biological processes on which they are based. It is important, however, to acknowledge uncertainty and to deal with it using the precautionary principle. Therefore, work of this type is likely to attract higher containment measures than would otherwise be applicable to the organisms on which they are based, or from which the genetic information has been derived."

- **USA National Institutes of Health Office of Biotechnology Activities**
  In 2013 the National Institutes of Health (NIH) changed its guidelines to include synthetic nucleic acids. Since, the "NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules" (NIH Guidelines) detail safety practices and containment procedures for basic and clinical research involving recombinant or synthetic nucleic acid molecules, including the creation and use of organisms and viruses containing recombinant or synthetic nucleic acid molecules.

- **Public Health Agency of Canada**
  The Canadian Biosafety Standards and Guidelines (Public Health Agency of Canada, 2013) include synthetic DNA and synthetic biology in the overview of the types of biological material that are important in the context of the standards and guidelines. In Chapter 4 on "Risk Groups, Containment Levels, and Risk Assessments" the following is indicated for synthetic Biology:
  > "The risks associated with synthetic biology and synthetic DNA technologies are similar to the risks associated with GMOs and rDNA technologies. The principal difference is that synthetic biology seeks to design and construct novel biological functions and systems not found in nature, and, as such, assessing the potential risks associated with products of synthetic biology is somewhat more complex."

Topic 6
Adequacy of national, regional and/or international instruments to regulate the organisms, components or products derived from synthetic biology techniques

At the regulatory level, the main conclusion that can be drawn to date is that current activities involving the development and use of synthetic organisms make use of techniques that fall within the scope of Directives 2009/41/EC and 2001/18/EC. In consequence the European

[7] Source: Synthetic Biology, Latest developments, biosafety considerations and regulatory challenges, Wetenschappelijk Instituut Volksgezondheid, September 2012, Belgium, D/2012/2505/46

GMO regulatory framework is for the moment adequate to support risk assessment of these activities. This applies also to cases where pathogenic micro-organisms are manipulated or reconstituted, since the scope of the Belgian legislation on contained use of GMOs also covers pathogens. However, it should be noted that some developments of SB (e.g. protocells or orthogonal systems) could raise potential issues as regard the regulatory status of the resulting organisms as these approaches could be considered as not leading to GMO or not meeting the definition of an organism in the meaning of the EU legislation[8].

Whether or not current instruments for the regulation of LMOs are adequate depends on a case-by-case assessment of the characteristics of the organism, and whether it meets the definition of a LMO.

It is important that research on societal impact is carried out to help identify new risks at an early stage and thus prevent possible undesirable developments from the very beginning. With respect to biological safety, the risks of current research within the field of synthetic biology have been appropriately identified and regulated within a legal framework. Some of the approaches used in synthetic biology even contribute to increasing biosafety through the management of the viability of genetically modified organisms[9].

The wealth of experience gained from several decades of assessing the risks of LMOs, and the long-established field of biosafety, remain relevant, and provide the foundational principles for the case-by-case assessment of the organisms developed with synthetic biology tools.

So far, the applications of synthetic biology concern processes conducted in controlled environments, such as fermenters. In this case, the long-established principles and procedures of biological containment apply, and the potential direct impact on biological diversity will be negligible.

One particular challenge in relation to the prediction of risks is that new biological systems created by synthetic biology may not have an appropriate 'comparator' organism. Current practice in the risk assessment of LMOs relies on comparisons with the non-modified equivalent organism. The absence of an appropriate comparator for an organism developed with synthetic biology tools does not in itself create a new risk, rather, more suitable approaches to risk assessment may need to be considered for such organisms. Such cases are already addressed in international documents like the Codex guidelines.

Topic 7

Degree to which the existing arrangements constitute a comprehensive framework in order to address impacts of organisms, components and products resulting from synthetic biology, in particular threats of significant reduction or loss of biological diversity

We believe that current agreements are adequate in so far as synthetic biology applications result in LMOs. For future synthetic biology applications, we believe that it is early days to develop new protocols.

[8] Source: Synthetic Biology, Latest developments, biosafety considerations and regulatory challenges, Wetenschappelijk Instituut Volksgezondheid, September 2012, Belgium, D/2012/2505/46

[9] Source: Synthetic Biology Statement, DFG, German Research Foundation, July 2009

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- UNEP/CBD/COP/12/INF/11 (2014) Note by the Executive Secretary - Potential positive and negative impacts of components, organisms and products resulting from synthetic biology techniques on the conservation and sustainable use of biodiversity, and associated social, economic and cultural considerations.
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