Special Report

Synthetic Biology

Policy & Implementation Issues

Synopsis of Seminar Series

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1. Introduction

The TransDisciplinary University (TDU) organized a series of special seminars on the topic of synthetic biology – policy and implementation issues during July – September 2017 in collaboration with United Nations Environment Programme (UNEP) and the Secretariat to Convention on Biological Diversity (SCBD).

Considering the ongoing discussions under the CBD on issues related to synthetic biology and in preparation for the Ad Hoc Technical Expert Group (AHTEG) meeting on synthetic biology and the 14th Meeting of Conference of Parties to the CBD that would consider policy and implementation issues related to synthetic biology and the related, the seminars focused on bringing together researchers, policy makers, industry, lawyers and academia to discuss key issues and contribute to the AHTEG and COP discussions as well as help Government of India prepare, nationally, to deal with policy and implementation issues related to synthetic biology.

The first seminar focused on review of recent technological developments within the field of synthetic biology and their impacts on biodiversity and environment, the second one on the question of whether synthetic biology organisms same as Living Modified Organisms and are there exceptions and the last one on making recommendations for CBD scientific body on synthetic biology and conservation, sustainable management of environment.

This report is a summary of discussions held during the three sessions and contains a set of follow up actions recommended at national and global levels.

2. Background

Synthetic biology (SB) has been garnering attention recently both for its innovative approaches to solving our health, development and related issues as well as impacts it will have on environment and socio economics. The Convention on Biological Diversity (CBD) and its Protocols namely, the Cartagena Protocol on Biosafety and the Nagoya

Protocol on Access to genetic resources and Benefit Sharing (ABS), have started focusing on understanding the technology and its impacts on environment and biological diversity.

With the Ad Hoc Technical Expert Group (AHTEG) having been established by the Parties to the CBD to provide an expert input to the Subsidiary Body on Scientific, Technical and Technological Advice (SBSTTA) who in turn will make recommendations to the fourteenth meeting of the Conference of Parties (COP) to the CBD in 2018, it is time for countries and stakeholder groups to discuss the implications of SB to the conservation and sustainable use of biodiversity and the fair and equitable sharing of benefits arising from the utilization of genetic resources.

The 13th Conference of Parties (COP13) of Convention on Biological Diversity (CBD) held in Cancun, Mexico noted the conclusion of the Ad Hoc Technical Expert Group (AHTEG) on Synthetic Biology (SB) that living organisms developed through current and near future applications of synthetic biology are similar to Living Modified Organisms (LMOs) as defined in the Cartagena Protocol. COP13 also noted that there is no clarity on whether some organisms which are currently in the early stages of research and development would fall under the definition of the living modified organisms under the Cartagena Protocol and there are cases in which there may be no consensus on whether the result of synthetic biology application is "living" or not. In this context, the second seminar of the Special Seminar Series on Synthetic Biology discussed the topic- "Synthetic Biology Organisms are LMOs- Are there any exceptions".

3. The Outcomes

Seminar # 1

"Review of recent technological developments within the field of synthetic biology and their impacts on biodiversity and environment".

Dr Balakrishna Pisuapti, Vice-Chancellor of TransDisciplinary University (TDU), highlighted the significance of the discussion on synthetic biology (SB) to understand where India is at the moment with respect to the subject. Even though a selected number of countries are participating in the

discussion, the implications are wide-ranging and will affect all Parties to the CBD and their actions related to SB. Multiple conventions including the Convention on Biological Diversity (CBD) and the Convention on Biological and Weapons of Mass Destruction have been deliberating the issues related to SB.

In parallel, EU has put together a European Academies paper on regulatory oversight and prioritization of stakeholders and in the US, through the US National Science Research Council has been working on both science and policy aspects related to SB. Dr Pisupati underlined the role of TDU in striving to bring about multiple stakeholders to discuss on the implications of the discussions by the CBD, in the context of preparing India and other countries to participate and decide on issues through the CBD processes. He maintained that the inputs from the seminars would contribute to the AHTEG and the online forum discussions and TDU will be proactive in contributing inputs to the Government of India and the Karnataka State Government in making relevant strategies at national and state levels.

Speaking on the science behind SB, Dr. S Ramaswamy, Professor and Dean, Institute for Stem Cell Biology and Regenerative Medicine, India, stressed the fact that advancements in science hold the key to improve the quality of human life. With respect to synthetic biology, Dr Ramaswamy was of the view that India has a remarkable opportunity because it is a megabiodiverse country. He went on to give a few illustrations of safe SB applications such as production of artificial dyes en-masse by bacteria without toxic end products, production of ursolic acid from gene strands of Holy Basil and the production of natural vanillin through yeast. The advanced applications of synthetic biology such as high protein bread and beer obtained by embedding gene strands from the embryonic sac of cockroach into yeast was also discussed. He ended his talk by drawing the attention to issues requiring thoughtful pondering, namely assessing the environmental impacts of a SB organisms and the regulatory mechanisms to handle SB organisms and products.

Highlighting the work of United Nations Environment (UNEP), Dr. Ileana Lopez, Programme Officer for Multilateral

Environmental Agreements, Division of Law and the Project manager for the implementation of the UNEP-GEF Biosafety Clearing House (BCH) project summarized the role and mandate of UNEP and the BCH in streamlining the policy surrounding SB. Dr. Ileana elaborated on the obligations of member and non-member nations under the Biosafety Clearing House (BCH). She also emphasized the need for information that needs to be made available if a country changes its regulatory frameworks in response to issues of SB. She also reminded the participants about links between debates under SB with those related to access and benefit sharing (ABS).

Dr. Manoela Miranda, Head of Biosafety and Biosecurity Unit at the Secretariat to the CBD walked the participants through the Cartagena protocol provisions that can apply to SB organisms as they are equated to Living Modified Organisms (LMOs) as concluded by the AHTEG and decided by CBD Conference of Parties in December 2016 (CBD COP 13). She also explained that the risk assessment principles that are in use for LMOs also serve as a basis for the risk assessment of SB organisms but risk assessment methodologies may need to be adapted current and future applications of SB. The operational definition of SB, as well as the use of the terms 'components', 'organisms' and 'products' that were laid out for bringing clarity to the deliberations.

Dr. Ezhil Subbian as a biotechnology professional working in the field of synthetic biology in India and Co-Founder of the biotech start-up, String Bio Private Limited provided the views from industry perspective. She spoke on the apprehensions shared by the industry in the country. The major challenge from a policy perspective, according to her, is in defining a new living organism developed through SB. Dr. Ezhil pointed out the current fields in which SB is being applied such as the production of meat in the lab. She explained the current work of her company, on creating sustainable products employing methane on a synthetic platform (STRING Integrated Methane Platform) creating SB solutions catering to the demands of local markets.

Speaking on behalf of Government of India and its initiatives, Dr. Sangita

Kasture, Joint Director, Department of Biotechnology, Ministry of Science & Technology of the Government of India) shared the perspectives and initiatives of the Department of Biotechnology (DBT) on synthetic biology including the Bioenergy program and highlighted current collaborations between India and its partners. She opined that the time has arrived for policy makers, the biotechnology industry and scientists in India to be a part of this global technological revolution. She shared hope that the outcomes of this series of seminars will help assist in framing the national policy on Synthetic Biology.

The presentations were followed by an open discussion moderated by Dr. Balakrishna Pisupati. The following are key points that were discussed during this session:

1. There is a need for better clarity and understanding of defining Synthetic Biology within the national context, considering the definition agreed to by CBD COP 13.
2. With an agreed definition, it is critical for all stakeholders, including the scientists and industry to use the same definition and terminology to avoid misunderstanding and misinterpretation of issues and components related to SB
3. India, with its current interest in investing in SB need to focus on collating and consolidating actions and actors working on SB in order to prepare a roadmap on SB investments and deployment.
4. There is need to understand 'components' that go into making SB organism and/or product. If so, mapping of the 'components' will be a key pre-requisite.
5. India needs to ensure its focus on SB related issues is not just current but future. Therefore, there is a need to develop a foresight analysis on SB as well as a national level strategy document on SB.
6. With communication taking centre stage in SB, it is important to develop a clear communication strategy to deal with using and scaling up SB organisms and products.
7. India needs to pro-actively participate in the ongoing CBD discussions and negotiations on SB and the DBT should work closely with the CBD focal point to ensure the priorities of India is appropriately

reflected in the CBD negotiations, and

8. TDU should continue its engagement in the process with full and informed participation of all stakeholders in the lead up to CBD COP 14 and beyond.

Seminar # 2

After recapping the main discussions from the first seminar, the presentation highlighted the pertinent questions that need to be deliberated, if SB Organisms are equated to that of LMOs: (1) Will the principles of biotechnology products and organisms apply to SB products and organisms? (2) Are countries prepared to deal with this under their existing risk assessment and management protocols? (3) What is the experience with SB organisms? The issues specifically for the Indian context are: Do we have scientific clarity on SB organisms and their behavior? Is there policy clarity on LMOs? Are the current protocols sufficient? It was pointed out that 'components' referred to parts used in a synthetic biology process like DNA molecule, and 'products' referred to the resulting output of a synthetic biology process like a chemical substance. The cardinal difference between Systems Biology and SB is in the process of engineering application of biological science in SB.

Mr. Shriram (Vice President, Evolva Biotech) spoke on the industry perspectives and the regulatory issues faced. He stated that SB derivatives fall broadly under two categories – 'Products' and 'Organisms'. Product refers to derivatives from an organism which acts as a 'producer' and 'enabler' while an organism may have new traits designed "*de novo*". Under the Products, there is a distinction between "Naturally unnatural" products and "Unnaturally natural" product. Artemisinin and Agarwood oil are examples of unnaturally natural products. Naturally unnatural products use a natural host but the final end product is unnatural. Few examples are SB based composite polymer for coating the inner chamber of submarines, propellers for unmanned drones and nano-drilling substances. The SB products are subjected to the relevant regulatory systems depending on the nature of the products (drugs, feeds, flavoring agents etc).

SB Organisms are two types- *De novo* and *In vivo*. *De novo* organisms are created from scratch and examples include (1) organisms that convert atmospheric pollutants to useful products (2) engineered bugs for biofouling, coated around the hulls of ships. *In vivo* organisms are self-replicating organisms. Issues with these are (a) containment risk and (b) ecological competitiveness. Countries like Switzerland have protocols and regulations such as Biosafety Locks (xenobiologics). From an industry perspective, he argues that SB product is the molecular output of a host cell, and host cells not being the final product will not be LMOs. The potential role of SB in reducing water footprints and carbon footprints were discussed. He concluded by outlining that SB offered a wide variety of benefits such as better economics, stable sustainable supply chains and consistent product qualities.

Mr. Shivakumar R (Partner, K&S Partners, Intellectual Property Firm) spoke on the legal aspects particularly patentability of the SB organisms and products. He discussed the patentability of SB organisms with respect to the aspects of traditional knowledge, patentability of animal/plant cells, method of agriculture, medical treatment and computer programs. The obligations by patent applicants to deposit biological material in the International Depository Authority under the Budapest Treaty were pointed out.

Dr. Ramaswamy (Dean, Institute for Stem Cell Biology and Regenerative Medicine) commented that SBOs and LMOs are treated as similar for international discussions, since both are based on recombinant DNA technology. He opined that SBOs can be different from LMOs in the context of having control circuits. For the purpose of regulation, however he gave two exceptions in which an SB organism require to be treated differently from LMOs:

1. The SBO possesses genes that do not exist in nature.
2. The SBO is an organism which has been entirely created from scratch.

The presentations were followed by an open discussion moderated by Sachin Sathyarajan and Alphonsa Jojan. The

following are key points that were discussed during this session:

1. **Regulatory aspects:** The need for regulation off 'process' along with the regulation of the 'product' was discussed. Processes require detailed examination as regulatory protocols exist in relation to the final product. An appropriate practice in the absence of well-defined protocols would be to embed Bio safety locks into the process.
2. **Access and Benefit Sharing:** The status of 'unnaturally natural' products from SB organisms as "biological resources" under the Indian Biological Diversity Act, 2002 needs clarification as currently they are referred as 'nature identical'. The disclosure requirement for origin of genetic resources and associated knowledge was deliberated.
3. **Livelihood Issues:** Based on the vanillin example, the impact on livelihoods was discussed in the context of replacement of natural products.
4. **Conservation and Sustainability:** The potential of SB to contribute towards augmenting conservation efforts can be explored especially in the context of herbal components of endangered species.

Seminar # 3

The outcomes of the previous two seminars on "Review recent technological developments within the field of synthetic biology and their impacts on biodiversity and environment" (21 July, 2017) and "Synthetic Biology Organisms are Living Modified Organisms – Are there Exceptions?" (4 August, 2017) were presented at the outset.

Presentations and key discussion points were made by the participants including, India's past and ongoing work related to synthetic biology, the science-policy-practice links, the policy environment, India's preparedness to participate in the CBD discussions as well as ways and means to map India's interest in the science and investment portfolio on synthetic biology.

The presentations were followed by a panel discussion on India's preparedness to deal with synthetic biology on further discussions to understand the definition of synthetic biology, as agreed to by the CBD, detailing the issue of equivalence (responding to the question – are

synthetic biology organisms same as living modified organisms?), understanding and taking stock of the tools and techniques as well as readiness from India in dealing with necessary assessments of synthetic biology organisms (and products) in relation to environment, economics and social aspects.

After detailed discussion, the following key points emerged:

1. Definition

The current definition, as agreed to under the CBD, was considered as adequate to deal with current and future interests from science and policy perspectives. Emphasis was made ensure stakeholders use the same definition and not create additional and/or new definitions to ensure clarity. However, it was agreed that 'future developments' and 'new dimensions' as provided for in the current definition of CBD needs careful review at national level[1]. Given the complexity of science and specificity of research on organisms and products, it was felt that there is a need to further consider the following four situations while dealing with synthetic biology

a. Developing organisms
b. Developing organisms that get used as products
c. Developing products, and
d. Developing derivatives.

It was suggested that CBD should consider the above situations while preparing for further discussions on synthetic biology.

2. Equivalence

Discussing the issue of equating synthetic biology organisms as living modified organisms (as suggested by the AHTEG in 2015 and decided by CBD COP 13)[2], participants realized the need for understanding the issue of equivalence between the synthetic biology organisms and living modified organisms be assessed on a case by case basis.

Sharing the experience of the industry, the participants realized that the issue of equivalence will be impacted both by

[1] Synthetic Biology is defined as '*Synthetic Biology is a further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding, design, re-design, manufacture and/or modification of genetic materials, living organisms and biological systems*' UNEP/CBD/Synbio/AHTEG/2015/1/3

[2] UNEP/CBD/COP/DC/ 13/17

the definition, science and tools available to deal with impacts. Therefore, it was agreed that recommendation be made to CBD to consider the issue of equivalence more seriously with a need to map out the method of creating/developing the organisms and their impacts in detail before the AHTEG meeting so that the discussions can be complete and robust.

In India, there was a recommendation to develop a national level matrix on mapping the tools and techniques before addressing the issue of equivalence.

3. Tools and readiness

Discussing the issue of readiness in the country to deal with synthetic biology organisms and products, the participants heighted the need for having a re-look at the current regulatory as well as policy frameworks to assess the availability of tools as well as readiness.

While agreeing to the need for reviewing the tools, the participants highlighted the need for consolidation of procedures and due diligence on issues such as generating safety data and assessments thereof.

The participants also discussed the links to Convention on Weapons of Mass Destruction (WMD), preparedness to deal with issues of accidental and unintentional release and the related.

4. Policy and regulatory aspects

Highlighting the issue of policy and regulatory preparedness in India to deal with synthetic biology organisms and products, the participants reviewed the current systems and frameworks and agreed that there is no immediate need to develop a new regulatory framework for India. However, it was felt that the current frameworks need to be reviewed and revised to accommodate the emerging issues related to synthetic biology.

For example, it was felt that the current mandate for Institutional Biosafety Review Committees can be expanded to also deal with and consider synthetic constructs and/or synthetic elements in addition to current LMO/GMO/rDNA needs.

It was also recommended that India needs to map out current actions related to synthetic biology – both by the private sector and public sector,

consider both organisms and products, develop a matrix of current and future developments and institutional mechanisms including overlaps and gaps within the regulatory and policy aspects.

The participants agreed to a suggestion on the need for a 'foresight analysis' on synthetic biology, wider consultations between various players working on and interested in synthetic biology, more coordination between the Department of Biotechnology (DBT), Government of India (that promotes and supports public sector actions related to synthetic biology) and the Ministry of Environment, Forests and Climate Change (MoEFCC), Government of India (the national focal point for the Cartagena Protocol on Biosafety and the CBD) in providing specific inputs to the CBD discussions besides developing a full-fledged communication strategy for synthetic biology on a priority basis.

It was felt that a national policy document on synthetic biology that considers the science, policy and practice elements will be needed soon to prioritize actions and encourage investments in this technology besides assessing the socio-economic implications of the technology and its products as well as the impacts on biodiversity.

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