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DIRECTORATE FOR SCIENCE, TECHNOLOGY AND INNOVATION
COMMITTEE FOR SCIENTIFIC AND TECHNOLOGICAL POLICY

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Working Party on Biotechnology

FUTURE POTENTIAL OF SYNTHETIC BIOLOGY IN BIO-BASED PRODUCTION
Results of a Survey

Delegates are invited to discuss this report at their next meeting on 4-5 December 2014 and send written comments to the Secretariat by 12 December 2014. After that date, any necessary amendments will be made and the report sent to the CSTP for declassification by written procedure.

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NOTE BY THE SECRETARIAT

The Programme of Work and Budget (PWB) 2013-2014 envisages a report on “Future Potential of Synthetic Biology in Biobased Production” under the theme of “Impact of Synthetic Biology on the Bioeconomy: Policies and Practices” (Output Result 1.3 of Output Area 1.3.3 - *Realising the potential of emerging, converging and enabling technologies: The impact on the bioeconomy of emerging/converging technologies*). A survey was conducted as one input to that report. This paper discusses the findings of that survey.

Delegates to the Working Party on Biotechnology are invited to:

- Discuss this draft survey report on the “Future potential of synthetic biology in biobased production”;
- Provide comments in writing by 12 December 2014; and
- Agree to the document subsequently being transmitted to the Committee for Scientific and Technological Policy for declassification by written procedure.

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EXECUTIVE SUMMARY

In order to explore issues associated with the use of synthetic biology in bio-based production, a survey was prepared for the Working Party on Biotechnology. This survey, to which 17 countries plus the EC responded,[1] is a first attempt to sketch the current landscape and give OECD countries an opportunity to review and consider aligning their goals for bioeconomies involving bio-based manufacturing. For countries new to synthetic biology, it is an opportunity to learn how other countries with more relevant experience are tackling policy issues. The survey was sent to delegates in 2013. This document reports the findings of the survey.

In brief, the survey concludes that:

- The challenge for countries is to find an official definition of synthetic biology that is of practical value yet sufficiently broad to allow for further developments in the field;

- R&D support for synthetic biology is available primarily through generic funding instruments. Only the US, UK and EU have funding initiatives dedicated to synthetic biology;

- Public-Private Partnerships covering synthetic biology or its incorporation into bio-based production are rare. Only the UK has PPPs focused on synthetic biology, though more countries have PPPs focused on bio-based production, some of which include synthetic biology elements;

- Despite speculation that synthetic biology might pose problems for intellectual property systems, none seem insurmountable and new mechanisms such as patent clearinghouses are being developed to cope with freedom-to-operate concerns;

- Many countries are developing demand-side mechanisms to stimulate the uptake of synthetic biology;

- Although lack of public acceptance and engagement are seen as potential barriers to the diffusion and use of synthetic biology, only a few countries have included, or are considering including, public engagement and communication elements in their overall strategies for the development and use of synthetic biology;

- A number of countries are evolving bioeconomy strategies, some are drawing up specific plans and roadmaps for the development of industrial biotechnology, and in a few instances there are dedicated attempts to exploit the potential of synthetic biotechnology in bio-production processes. The challenge, however, is to ensure the close alignment of these initiatives if the full potential of synthetic biotechnology is to be realised.

- In terms of future policies, countries are expected to:

[1] In addition to the European Commission, responses were received from: Austria, Belgium (Flanders and Brussels region), Canada, the Czech Republic, Denmark, Germany, Italy, Japan, Mexico, Norway, Portugal, the Russian Federation, South Africa, Slovenia, Switzerland, the United Kingdom and the United States of America.

- Stimulate synthetic biology research in dedicated centres of excellence, with dedicated programmes linked to the development of the bio-economy;
- Ensure that legislation and regulation enable the uptake of products developed through synthetic biology, including safety regulation and IP issues;
- Engage with the public to make synthetic biology understandable and highlight potential benefits;
- Provide incentives for existing companies and start-ups to engage in technology transfer and commercialisation activities.

THE FUTURE POTENTIAL OF SYNTHETIC BIOLOGY IN BIO-BASED PRODUCTION: RESULTS OF A SURVEY

Introduction

1. The term 'synthetic biology' is now in common use, appearing in the United States (US) National Bioeconomy Blueprint (The White House, 2012) twenty one times, eighteen times in the main text and three times in footnotes. In reports of the German Bio-Economy Research and Technology Council, the term appears eight times in *Bio-economy Innovation* (BÖR 2010) and four times in *Priorities in Bio-economic Research* (BÖR, 2011). Similarly, in *A synthetic biology roadmap for the UK* (United Kingdom (UK) Synthetic Biology Coordination Group, 2012), the term 'bioeconomy' appears seven times.

2. Within a bioeconomy, stakeholders are seeking to reduce dependence on fossil resource consumption and address the issue of climate change mitigation, in part through industrial biotechnology. Synthetic biology has the potential to play a significant role in overcoming barriers in industrial fermentation and expanding the number of chemicals and fuels that can be produced. Thus, a central position for synthetic biology in a new industrial revolution can be seen in which bio-manufacturing becomes entrenched. The bioeconomy, industrial biotechnology and synthetic biology have therefore become closely linked.

3. The OECD chemicals sector is large and vital to the economy, but a major weakness is that very few member countries have large fossil fuel reserves of their own and the vast majority of chemicals are made from fossil resources (oil and gas). Just as oil and petrochemicals are essential global commodities, it is anticipated that climate change and dwindling fossil resources will result in bio-based equivalents eventually becoming such commodities too. OECD countries are still likely to play a major part in this new economy, one in which biotechnology will play a central role in manufacturing.

4. A new industrial revolution, with biomass as a key source of raw materials instead of oil, has the potential to alleviate the problem of energy security in OECD countries. The concentration of much of the world's expertise in synthetic biology in the OECD countries is another advantage. That said, some countries will inevitably be in a more advantageous position than others. Many OECD countries have limited supplies of biomass, but synthetic biology has the potential to increase the efficiency of its utilisation.

5. It is still very early in the development of manufacturing processes that use synthetic biology and this is a critical time. As biorefineries are being built and the earliest synthetic biology research infrastructure is being deployed, OECD governments could reflect that this is a period of opportunity. Ignoring these developments could exclude countries from a new manufacturing revolution and leave them in a state of resource insecurity.

6. In order to explore issues associated with the use of synthetic biology in bio-based production, a survey was prepared for the Working Party on Biotechnology. This survey was a first OECD attempt to sketch the current landscape and to give the OECD countries an opportunity to align their goals for a bioeconomy involving bio-based manufacturing. For countries new to synthetic biology, it is an opportunity to learn how other countries with more relevant experience are tackling policy issues. The survey was sent to delegates in 2013. This document reports the findings of the survey.

Scope of the survey

7. The future potential of synthetic biology in bio-based production in any country will depend on a number of factors. These include, for example:

- Aspirations concerning the development of a bioeconomy, with bio-based production playing a central role;
- The availability of R&D support (for pre-competitive research);
- Support for post-'proof-of-concept' R&D e.g. demonstrator plant design and construction;
- A strategy for scale-up and infrastructure development, which will probably rely on public-private partnerships (PPPs);
- The future nature and direction of intellectual property developments in the life sciences, especially those specifically associated with synthetic biology;
- Attention to demand-side aspects, such as readying markets for new products and public procurement;
- Careful attention to public engagement.

8. The survey was designed to discover, at the country level:

- If there is as an awareness of the role synthetic biology might play in the bioeconomy strategies being developed by countries, and also if bioeconomy strategies are coordinated with synthetic biology roadmaps;
- What policy measures are critical to the development of synthetic biology e.g. R&D support, intellectual property, public engagement.

9. The survey (see Annex 1) was sent to delegates of the Working Party on Biotechnology (WPB) and the Task Force on Industrial Biotechnology (TFIB). Responses were received from seventeen countries and the European Commission (EC), covering 21 ministries or organisations. Responses were received from Austria, Belgium (Flanders and Brussels region), Canada, the Czech Republic, Denmark, Germany, Italy, Japan, Mexico, Norway, Portugal, the Russian Federation, South Africa, Slovenia, Switzerland, the United Kingdom (UK), the United States (US) and the EC.

Results of the Survey

Bioeconomy and synthetic biology – definitions and strategies

10. Only two countries (South Africa and the UK) reported having an official definition of synthetic biology. In the European Union, a definition is under development for legislative purposes, while a working definition from the ERA-NET ERASynBio[2] is being used within the EC and by ERA-NET participants such as Germany, Italy and Norway. Some countries, including Canada, base their definition on that of the UK Royal Society, which is:

"*Synthetic biology involves the design and construction of novel artificial biological pathways, organisms and devices or the redesign of existing natural biological systems*."

11. While not the official position of the Government of Canada, a governmental working group on synthetic biology has developed a working definition based on the Royal Society definition that is used solely for internal deliberations.

12. The Engineering Research Centre, SynBERC, of the US NSF (National Science Foundation) has had a standing definition for approximately seven years.[3] The US Biotechnology Industry Organisation (BIO) has also had a definition on its website for the past seven years.[4]

13. Box 1 shows, from the literature, some definitions and opinions concerning the nature of synthetic biology.

Box 1. Some published definitions of, or opinions on, synthetic biology.

Blake and Isaacs (2004)

Synthetic biology is advancing rapidly as biologists, physicists and engineers are combining their efforts to understand and programme cell function. By characterising isolated genetic components or modules, experimentalists have paved the way for more quantitative analyses of genetic networks.

Benner and Sismour (2005)

[Synthetic biology] attempts to recreate in unnatural chemical systems the emergent properties of living systems … [the] engineering community has given further meaning to the title…to extract from living systems interchangeable parts that might be tested, validated as construction units, and reassembled to create devices that might (or might not) have analogues in living systems.

NEST (2005b)

Synthetic biology is the engineering of biological components and systems that do not exist in nature and the re-engineering of existing biological elements; it is determined on the intentional design of artificial biological systems, rather than on the understanding of natural biology.

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2 www.erasynbio.eu/project. ERASynBio released a document in April 2014 with a definition of synthetic biology: ERASynBio (2014). Next steps for European synthetic biology: a strategic vision from ERASynBio.

3 www.synberc.org/what-is-synbio

4 www.bio.org/articles/synthetic-biology-explained

De Vriend (2006)

Synthetic biology is a new emerging scientific field where ICT, biotechnology and nanotechnology meet and strengthen each other. Synthetic biology is a new trend in science and technology and a clear example of converging technologies.

Heinemann and Panke (2006)

Synthetic biology is interpreted as the engineering-driven building of increasingly complex biological entities for novel applications.

Drubin et al. (2007)

Synthetic biology refers to a variety of experimental approaches that either seek to modify or mimic biological systems.

ETC (2007)

Definition: Synthetic Biology (also known as Synbio, Synthetic Genomics, Constructive Biology or Systems Biology) – the design and construction of new biological parts, devices and systems that do not exist in the natural world and also the redesign of existing biological systems to perform specific tasks. Advances in nano-scale technologies – manipulation of matter at the level of atoms and molecules – are contributing to advances in synthetic biology.

Royal Society (2007)

Synthetic biology is an emerging area of research that can broadly be described as the design and construction of novel artificial biological pathways, organisms or devices, or the redesign of existing natural biological systems.

Entus et al. (2007)

Synthetic biology is a useful tool to investigate the dynamics of small biological networks and to assess our capacity to predict their behaviour from computational models.

Bunn (2008)

Synthetic biology aims to design and build new biological parts and systems or to modify existing ones to carry out novel tasks.

IRGC (2008)

Most definitions of synthetic biology have two parts: synthetic biology is defined as the construction of completely novel biological entities, and the re-design of already existing ones.

TESSY (2008)

Synthetic biology uses nucleic acid elements or complex systems that are predefined and chemically synthesised in the laboratory by a modular approach. This approach aims to: 1. engineer and study biological systems that do not exist as such in nature, and 2. use this approach for: *i)* achieving better

understanding of life processes; *ii)* generating and assembling functional modular components; *iii)* developing novel applications or processes.

De Lorenzo and Danchin (2008)

The fundamental idea behind synthetic biology is that any biological system can be regarded as a combination of individual functional elements — not unlike those found in man-made devices. These can therefore be described as a limited number of parts that can be combined in novel configurations to modify existing properties or to create new ones.

EGE (2009)

A definition of synthetic biology should therefore include: 1. The design of minimal cells/organisms (including minimal genomes); 2. The identification and use of biological 'parts' (toolkit); 3. The construction of totally or partially artificial biological systems.

Parens et al. (2009)

To advance knowledge and create products that can promote human welfare, synthetic biologists seek to create biological systems that do not occur naturally as well as reengineer biological systems that do occur naturally.

The Royal Academy of Engineering (2009)

Synthetic biology aims to design and engineer biologically based parts, novel devices and systems as well as redesigning existing, natural biological systems. Synthetic biology strives to make the engineering of biology easier and more predictable.

Bayer (2010)

Synthetic biology is the design and construction of biological systems guided by engineering principles, with the aim of understanding biology or producing useful biological technologies.

PCSBI (2010)

Synthetic biology is the name given to an emerging field of research that combines elements of biology, engineering, genetics, chemistry, and computer science.

HSE (2012)

Synthetic biology is a term used to cover areas of biochemistry research that is involved in the chemical synthesis of DNA, utilising biological agents or their components for potential application across a wide range of industrial sectors.

UK Synthetic Biology Roadmap Coordination Group (2012)

Synthetic biology is the design and engineering of biologically based parts, novel devices and systems as well as the redesign of existing, natural biological systems.

ERASynBio (2014)

Synthetic biology is the engineering of biology: the deliberate (re)design and construction of novel biological and biologically based parts, devices and systems to perform new functions for useful purposes,

that draws on principles elucidated from biology and engineering.

South Africa

Synthetic biology can be defined as the process of utilising, redesigning and/or reassembling biological structures in the synthesis of advanced devices and materials for applications in medicine, energy, the environment and industry.

UK Synthetic Biology Leadership Council

Synthetic Biology (SynBio) applies engineering principles to biology to enable the design and synthesis of standardised and well understood biological parts which, in turn, can be used to develop biological devices and systems with potential future applications ranging from energy to healthcare.

Source : Various, as identified in the text

14. Eight countries (Belgium, Canada, Germany, Italy, Norway, the Russian Federation, South Africa and the US) and the EC have, or are developing, a bioeconomy strategy (see Figure 1 and Figure 3). In four of these (Germany, Italy, South Africa and the US) the strategy envisages bio-based production using synthetic biology. In Canada, the Russian Federation and the EC, the strategies include synthetic biology as one type of novel technology, although no explicit reference is made to bio-based product development through synthetic biology. In Norway, the development of a bioeconomy strategy is still at an early stage and it is not clear yet whether synthetic biology will be specifically addressed.

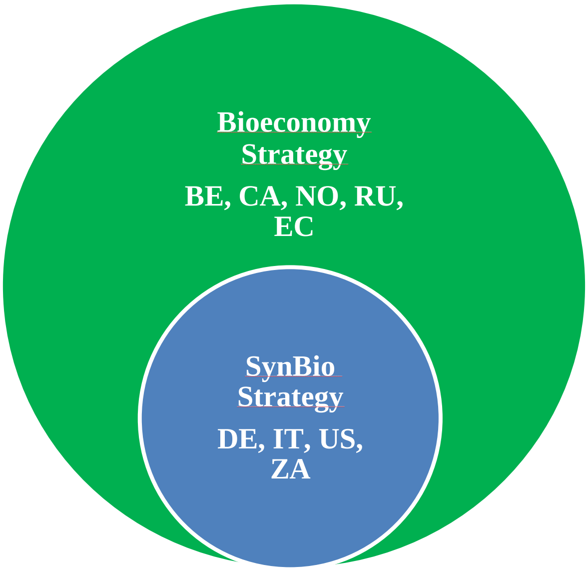
15. The US' government released its Bioeconomy Blueprint on 26 April 2012. It outlines the US strategy for economic revival based on a technological lead in agriculture, biotechnology, health sciences and entrepreneurship.[5,6] The US bioeconomy strategy includes the use of synthetic biology techniques for bio-based production. In addition, the Lawrence Berkeley National Laboratory has a ten-year strategic plan, one component of which is a BioManufacturing strategy.[7]

5 www.ascension-publishing.com/BIZ/Bioeconomy-Blueprint.pdf

6 www.whitehouse.gov/blog/2012/04/26/national-bioeconomy-blueprint-released

7 http://biosciences.lbl.gov/strategic-plan/

Figure 1. Bioeconomy and synthetic biology strategies



16. While the UK does not have a specific bioeconomy strategy, the UK Government launched a life sciences strategy[8] in 2011 that aims to develop an environment and infrastructure in the life sciences industry that supports researchers and clinicians to bring innovation to market earlier. It covers many of the same issues as a bioeconomy strategy.

Synthetic biology roadmaps

17. While it has no specific bioeconomy strategy, the UK does have a well-developed roadmap for synthetic biology (UK Synthetic Biology Coordination Group, 2012) (Q5, Q6). The potential of synthetic biology and the role of government in helping to develop a world-leading synthetic biology sector in the UK were addressed specifically, in October 2011, at a roundtable chaired by the Secretary of State for Business, Innovation and Skills (BIS) and the Minister for Universities and Science. The UK government has recognised the potential of synthetic biology as one of the key platform technologies to underpin growth and create new jobs (Box 2) in a 'low carbon'/green economy[9] and this is underlined by its inclusion as one of the eight Great Technologies[10].

18. Subsequent to the roundtable, the UK Synthetic Biology Roadmap Coordination Group was facilitated by BIS to draw up a synthetic biology roadmap. This was launched in July 2012, with five overarching recommendations:

- Establish a Synthetic Biology Leadership Council;
- Invest in a network of multidisciplinary centres to establish UK synthetic biology resource;
- Build a UK-wide synthetic biology community;
- Invest to accelerate technology deployment to market responsibly; and

8 www.gov.uk/government/publications/uk-life-sciences-strategy

9 www.hm-treasury.gov.uk/speech_chx_091112.htm

10 www.gov.uk/government/speeches/eight-great-technologies

- Assume a leading international role.

19. The Synthetic Biology Leadership Council (SBLC)[11] has since been formed. It is a strategic governance body that aims to assess progress, update recommendations and shape priorities for implementation of the roadmap. It also provides a visible point for strategic coordination between funding agencies, the research community, industry, government sponsors and other stakeholders, including some with societal and ethical priority interests.

Box 2. The UK synthetic biology roadmap and a vision for commercialisation

Seeing the opportunity: An opportunity exists to bring those at the cutting edge of science together with innovators in business to find the best fit between commercial opportunity and scientific potential, and to help them to work together to develop their ideas: to energise the new product supply chain, and to inform the science base.

Creating the industrial translation process: It is essential to develop processes whereby industrialists and academic researchers can more effectively collaborate to define application projects and requirements in terms of industrial techniques, market potential and societal benefits.

Accelerating the journey to market: Each organisation along the value chain has to evaluate the impact a new technology may have on its operations. One of the best ways to speed up this process is to create 'demonstrators' that show what is on offer in a compelling way. Helping innovating organisations to produce demonstrators of various kinds will advance the technology more quickly to market.

Reducing the commercial and technical risk: This can be done by bringing people from different organisations and with different capabilities together to work jointly on collaborative projects. These organisations can find better solutions to problems, and share the research and development costs, reducing the burden on any individual one of them.

Building a community of practitioners: When businesses cluster together, they can collectively be more effective. A characteristic of synthetic biology is the need for multidisciplinary centres. Establishing a wide network of academic, industrial and other organisational interests will benefit from the presence of a backbone of potentially several multidisciplinary centres.

Intellectual property: At a fundamental level, the concept of 'ownership' of living organisms and components raises ethical and legal issues that are approached differently in different jurisdictions. At a technology level, there needs to be a balance between that which may reasonably be protected and that which would encourage greater enterprise through being made available as open source.

Source : UK Synthetic Biology Coordination Group (2012)

20. In the Russian Federation, synthetic biology is included in the roadmap "Development of Biotechnologies and Genetic Engineering", supported by the Ministry of Economic Development. In Italy, a roadmap for synthetic biology is under development. Germany and Norway both refer to the roadmap that is under development in the context of the ERASynBio network (see Box 3). In Canada, a working group on synthetic biology is examining the regulatory and policy framework to guide the federal government to identify risks associated with synthetic biology. A roadmap may be developed in

11 https://connect.innovateuk.org/web/synthetic-biology-special-interest-group/synbio-leadership-council

the future. The responses to a question on the coverage in roadmaps of applications of synthetic biology are summarised in Table 1.

Table 1. Envisaged applications of synthetic biology

	Country			
Application	CA	DE	RU	UK
Agriculture	●	●	●	●
Bioenergy		●	●	●
Biomedicine	●	●		●
Environmental	●	●	●	●
Biosensor	●	●		●
Chemicals		●	●	●
Plastics		●	●	●
Marine	●	●		●
Roadmap			●	●

21. Germany and the UK envisage applications of synthetic biology in all fields listed in the questionnaire, while, in Canada, bioenergy, chemistry and plastics are not envisaged as applications. The Russian Federation does not consider biomedicine and biosensors in their roadmap for synthetic biology. In Belgium, the development of a roadmap "to tackle emergent research challenges (at the interface of synthetic biology and systems biology) in a systematic way with clear goals, milestones and suitable measures" is under development by SYNCELLS, an international scientific research network that is supported by the Research Foundation of Flanders[12].

22. A roadmap for synthetic biology is encompassed within Horizon 2020 - The New European Framework Programme for Research and Innovation (2014-2020). It includes the support of cutting-edge biotechnologies such as synthetic biology, bioinformatics and systems biology, and it envisages exploiting convergence with other enabling technologies such as nanotechnology and ICT (e.g. in bioelectronics).

Box 3. The ERASynBio vision for synthetic biology, April 2014

The ERASynBio project was supported national governments and the EC within the context of the Seventh Framework Programme. In April 2014, project participants released a document called "Next steps for European synthetic biology: a strategic vision from ERASynBio".

The ERASynBio vision predicts that the greatest **economic impacts** in Europe will be in:

- Industrial biotechnology and bioenergy;
- Medicine;
- Ecology and agriculture; and
- Materials science.

12 http://bioi.biw.kuleuven.be/syncells/about.html

In turn, the greatest **societal impacts** are envisaged in:

- Lifelong health and wellbeing: meeting the challenges of the ageing population in Europe and the widening gap between lifespan and wellbeing;
- Energy security, living with and avoiding environmental change: ensuring access to affordable and sustainable energy for a growing population, while mitigating the effects of climate change; and
- Global food security: providing the world's growing population with a sustainable and secure supply of nutritious food from less land and using fewer inputs.

During the development of this vision, five thematic areas were consistently identified as key to the development of a European synthetic biology research base capable of delivering on these opportunities:

Theme 1: World-leading and innovative synthetic biology research

Theme 2: Responsible research and innovation

Theme 3: A networked, multidisciplinary and transnational community

Theme 4: A skilled, creative and interconnected workforce

Theme 5: Cutting-edge open data and technology

Source : ERASynBio (2014)

R&D support for synthetic biology

23. Except for the UK and the US, in most countries there are no dedicated national or regional calls for research projects using synthetic biology. In total, over GBP 120 million (USD 200 million) has been committed to synthetic biology research and development in the UK. The Biotechnology and Biological Sciences Research Council (BBSRC) is leading the implementation of an integrated 'Synthetic Biology for Growth' package with the Engineering and Physical Sciences Research Council (EPSRC), the Economic and Social Research Council (ESRC), the Medical Research Council (MRC) and the Technology Strategy Board (TSB, the UK innovation agency)[13].

24. The US Defense Advanced Research Projects Agency (DARPA) has had multiple calls in synthetic biology (see Box 4).[14] In addition, the National Science Foundation (NSF) ERC Programme has provided funding for SynBERC, a multi-university research centre established in 2006 to help lay the foundation for synthetic biology in the US. The core university partners of SynBERC are UC Berkeley, UC San Francisco, Stanford, Harvard and MIT. SynBERC also has a large number of industry partners. Engagement between academia and industry should help to facilitate technology transfer and lead to the commercial use of the research results of the centre. The mission of SynBERC is:

- To develop the basic knowledge and tools to design and assemble biological systems to accomplish many complex tasks;
- To train a new cadre of researchers who will specialise in synthetic biology; and
- To develop and share best practices for the safe and ethical development of the field.

13 www.innovateuk.org/

14 www.darpa.mil/Our_Work/BTO/Programs/Living_Foundries.aspx

25. The NSF Molecular Section is starting coordinated calls in synthetic biology and has invited members from the Synthetic Biology Working Group of the Biotechnology Industry Organisation (BIO) for discussions. A large amount of funding related to biofuels has been set to address synthetic biology approaches.

Box 4. A summary of US initiatives in synthetic biology

Defense Advanced Research Projects Agency (DARPA): following on DARPA's Living Foundries programme (especially the 1 000 Molecules and ACTG components),[15] DARPA announced at the beginning of April 2014, that it is creating a major new advanced research organisation within DARPA called the Biological Technologies Office (BTO).[16] The BTO will coordinate DARPA's growing portfolio of R&D for synthetic biology. (The ACTG component is developing new tools and technologies to accelerate the biological design-build-test cycle. The 1 000 Molecules component seeks to build a scale, integrated, rapid design and prototyping infrastructure in the US for engineering biology and enabling synthetic biology with numerous applications). The government is also creating a new budgetary programme under DARPA, called Advanced Capabilities in Engineering Biology (ACE) that will be focused primarily on synthetic biology as a high growth area for US technology.

National Institute of Standards and Technology (NIST) is developing standards, characterisation techniques and reference materials for biochemical domains with a focus on standards and references for synthetic biology. The FY 2015 budget requests USD 8 million to ensure quality and predictability in the design of synthetic biological systems for efficient production of fuels, chemical feedstocks, pharmaceuticals and medical therapies. NIST has also has created a new centre at Stanford and it has been working with the BioBricks Foundation (BBF) to develop approaches for the field of synthetic biology.

Department of Energy (DOE) is supporting a broad range of new initiatives and tools development in synthetic biology as part of its mission to explore the frontiers of genome-enabled biology and to undertake multi-scale explorations for systems understanding of biology. Those involving synthetic biology include: DOE Bioenergy Research Centres; work on biosystems design for biofuels production; the DOE Systems Biology Knowledgebase (KBase) for enabling predictive biology in synthetic biology; the development of new methods and technologies for Biosystems Design essential for synthetic biology; and new computational tools and bioinformatics for synthetic biology.

National Institutes of Health (NIH): has created two National Centres for Systems and Synthetic Biology at UCSF and MIT. It is also planning new support for synthetic biology and biodiversity and for natural products development using synthetic biology.

The US Agricultural Act of 2014 signed by President Obama in February 2014 provides USD 700 million in funding for research at the National Institute of Food and Agriculture (NIFA) and the Agricultural and Food Research Initiative (AFRI).[17] Research applications of synthetic biology in agriculture and food are considered a priority area for genomics-related USDA research into specialty crops and new agricultural techniques.

National Science Foundation (NSF) continues to fund a broad range of research related to synthetic biology. It also supports the development of tools, data, and computational technologies essential for enabling the growth of synthetic biology. Finally, it funds educational training and support for those

15 www.darpa.mil/Our_Work/BTO/Programs/Living_Foundries.aspx

16 www.darpa.mil/NewsEvents/Releases/2014/04/01.aspx

17 https://agriculture.house.gov/bill/agricultural-act-2014

involved with synthetic biology.

Federal Bureau of Investigation (FBI): The FBI is taking proactive measures to bring biosecurity issues to the public and to the synthetic biology community. For example, the FBI now sponsors a security prize at the iGEM annual competition. The FBI also receives suspect DNA synthesis requests from companies and investigates further to see if any legal intervention is required. They have also coordinated this activity with Interpol.

Initiatives of the National Academies

The NAS Forum on Synthetic Biology: creation of a new 12-15 member National Academy of Sciences Forum on Synthetic Biology serving as a national co-ordinating group for all issues related to synthetic biology.

The NAS/National Research Council study on the "Industrialisation of Biology": major new initiatives and a research report to the US government about the critical role of synthetic biology in US next-generation manufacturing/production economy. The initial report will focus on advanced chemicals and is called "the Industrialisation of Biology". It is a cross-cutting and joint effort between the NAS Board on Life Sciences and the NAS Board on Chemical Sciences and Technology.

The NAS Convergence project: a new NAS project about new security (economic, geopolitical, etc.) issues related to the bioeconomy and synthetic biology called "Convergence: Securing Technology in the Bioeconomy". It will focus on new security issues related to synthetic biology, global value and supply chains, and new processes.

The NAS Enabling Architecture for Next-Generation Life Sciences Infrastructure project: a new NAS project on next-generation infrastructure for the life sciences that will focus heavily on infrastructure and non-application specific tools, standards and data for enabling synthetic biology.

Foundations, non-governmental organisations, and companies

The **BioBricks Foundation (BBF)**, the umbrella group for the synthetic biology community, has created four major new tools and initiatives to promote openness in synthetic biology and to provide enabling tools for those working in synthetic biology. They include:

- The BioBricks Public Agreement (BPA) for intellectual property and sharing biological parts;
- The Biobrick Public Agreement Plasmid Collection;
- The BIOFAB kit for using biological parts; and
- A widely used on-line tool called OpenWetWare.

The BBF and Stanford University have created the Stanford **BIOFAB** to create and widely distribute a collection of genetic parts. For example, BIOFAB parts can be reused in combination with novel genes to achieve very precise and different expression levels and to make a plethora of materials - for health, fuels, and chemicals.

The Semiconductor Research Corporation (SRC)[18] has launched the **Semiconductor Synthetic Biology (SSB) research programme** for next-generation bio-semiconductor systems at six American universities. The semiconductor industry believes that synthetic biology may play a major role in next-generation semiconductors and information technologies by providing critical new circuit designs, bio-electric sensors

18 www.src.org/

and actuators, and molecular-precision Additive Fabrication at the nanometre scale found in basic biology.

A number of US universities are creating **new centres for synthetic biology**, such as the MIT Centre for Integrative Synthetic Biology and the Stanford Synthetic Biology Centre. US universities are offering an expanded range of course offerings in synthetic biology at the undergraduate and graduate level, and synthetic biology is no longer confined to science and engineering courses. Many of the new courses involve courses and programmes on synthetic biology as a new basis for design, a range of social science and bioethics courses related to synthetic biology, and many new multi-disciplinary curricular offerings and degree programmes in synthetic biology such as those recently pioneered at Brown and at Rice.

Source : Courtesy of R Johnson, BIAC

26. One out of the four largest single public research grants ever given in Denmark (each of approx. DKK 120 million (USD 22 million) from the Strategic Research Council's programme for strategic growth technologies[19]) went to synthetic biology research after an open call in 2008 called "UNIK – Universities' Investment Capital".

27. UNIK synthetic biology at the University of Copenhagen was one of four cross-disciplinary research initiatives to receive UNIK grants in 2009. The start of the UNIK synthetic biology project at the University of Copenhagen marked the beginning of synthetic biology research in Denmark.[20]

28. Denmark, Germany, Italy, Norway and Portugal allocate funding for dedicated calls related to synthetic biology through the ERASynBio ERA-NET. The other countries support research involving synthetic biology through their general funding agencies or programmes. The ERASynBio project mobilised around EUR 15.5 million in a first call "to build synthetic biology capacity through innovative transnational projects". Table 2 gives an overview of the contribution of funding agencies/ministries involved in this call. Fifty five project proposals were submitted and eight were selected for funding. The second call had a budget of approximately EUR 16 million. The same funding agencies/ministries supported the call (apart from the Austrian Science Fund), plus MINECO, the Ministry of Economy and Competitiveness[21] in Spain, and MIZS, the Ministry of Education, Science and Sport of Slovenia.

19 http://fivu.dk/en/research-and-innovation/councils-and-commissions/the-danish-council-for-strategic-research/about-the-council/the-programme-commissions/programme-commission-on-strategic-growth-technologies

20 http://synbio.ku.dk/project_list/unik/

21 www.mineco.gob.es/portal/site/mineco/?lang_choosen=en

Table 2. Funding agency, country and budget for research projects in ERASynBio

Funding organisation, Country	**Preliminary budget (MEUR) Call 1**	**Preliminary budget (MEUR) Call 2**
AKA (Academy of Finland, Finland)	1.0	0.8
ANR (National Research Agency, France)	1.0	1.5
BBSRC (Biotechnology and Biological Sciences Research Council, UK)	3.0	3.0
BMBF (Federal Ministry of Education and Research, PTJ, Germany)	3.0	3.0
DASTI (Danish Agency for Science, Technology and Innovation, Denmark)	0.5	1
FCT (Foundation for Science and Technology, Portugal)	0.2	0.2
FWF (The Austrian Science Fund, Austria)	0.5	
KTI (Commission for Technology and Innovation, Switzerland)	1.5	0.5-1.0
LAS (Latvian Academy of Sciences, Latvia)	0.3	0.3
MESS (Ministry of Education, Science and Sport, Slovenia)	0.6	0.42
MINECO (Ministry of Economy and Competitiveness, Spain)		0.4
NSF (National Science Foundation, USA)	2.0	3.0
RCN (Research Council of Norway, Norway)	1.4	1.5
Total	**15.5**	**16.0**

29. A major funding source for synthetic biology research in Europe was the Seventh Framework Programme (FP7). Close to EUR 49 million was used for the co-funding of 13 projects involving synthetic biology (total cost EUR 67.63 million) between 2007 and 2013.

30. In the first Horizon 2020 call for proposals, launched on 11 December 2013, EUR 18 million was earmarked for synthetic biology research towards "the construction of organisms for new products and processes"[22].

31. Public funding for R&D in synthetic biology (see Table 3) in many regions (the European Union plus nine countries – Canada, Germany, Italy, Mexico, Portugal, the Russian Federation, South Africa, the UK and the US) is focused on applications to develop and produce bio-based products. In eight countries, public funding of R&D also supports basic research (Belgium, Canada, the Czech Republic, Germany, Mexico, Portugal, the UK and the US) and enabling technologies (Belgium, Canada, Germany, Italy, Mexico, Portugal, South Africa, the UK and the US). Only four countries (Portugal, the Russian Federation, the UK and the US) fund scale-up projects related to synthetic biology and five

22 http://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/topics/2596-biotec-1-2014.html

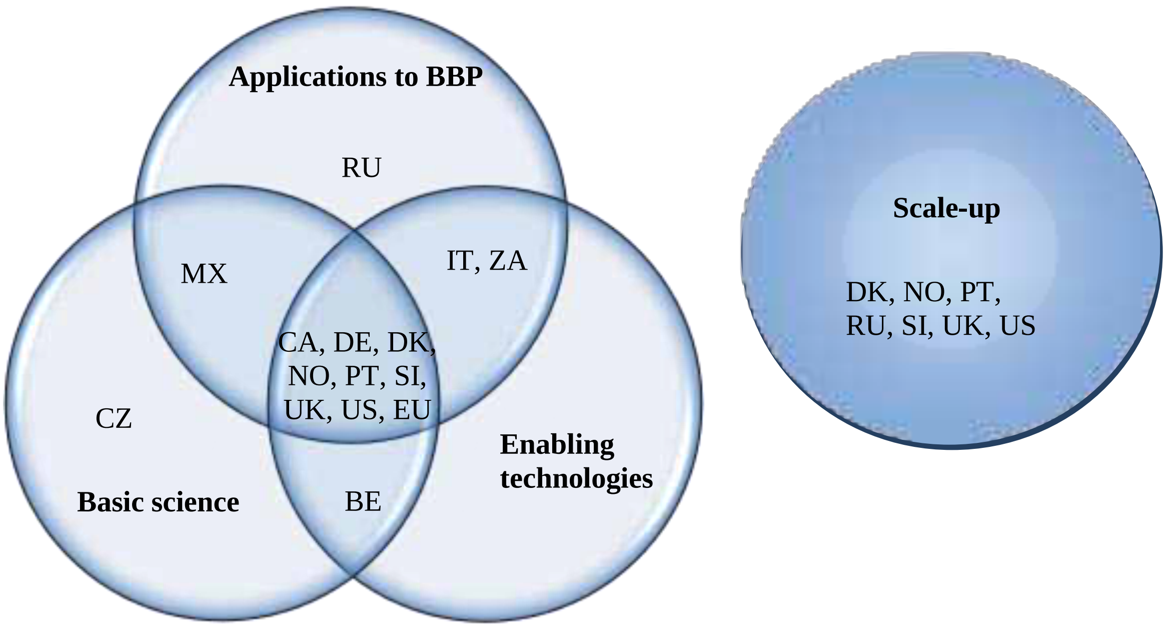
respondents (Canada, Denmark, Norway, Slovenia and the European Union) report that there is public funding for a mixture of these different categories of research involving synthetic biology. Canada, the UK and the US foresee public funding for each of the different categories of research with respect to synthetic biology.

Table 3. Public funding for support in different phases of the value chain.

Country	Basic science	Enabling technologies	Applications to BBP*	Scale-up	Mixture
BE	●	●			
CA	●	●	●		●
CZ	●				
DE	●	●	●		
DK					●
IT		●	●		
MX	●		●		
NO					●
PT	●	●	●	●	
RU			●	●	
SI					●
UK	●	●	●	●	
US	●	●	●	●	
ZA		●	●		
EU			●		●
Total	8	8	9+1	4	4+1

*BBP = bio-based production

Figure 2. Public funding for support in different phases of the value chain



32. In the US, public funding for R&D that focuses on applications of synthetic biology mainly addresses advanced biofuels and other clean energy technologies. As of February 7 2014, the enactment of the 2014 Farm Bill (Agriculture Act of 2014) has opened manufacturing programmes for the very first time to renewable chemicals and bio-based products. In addition, for the first time, the definition of renewable chemicals is in the 2014 Farm Bill. In previous Farm Bills, these programmes were only for advanced biofuels. Now some are open to renewable chemicals and bio-based products, including the Biorefinery Assistance Program (renamed the Biorefinery, Renewable Chemical, and Biobased Product Manufacturing Assistance Program)[23] and the multi-agency Biomass Research and Development Initiative.[24]

33. Most countries have policies and public funding to support the development of research infrastructure, including centres of excellence, or to stimulate international collaboration (Belgium, Canada, the Czech Republic, Denmark, Italy, Russia, Slovenia, South Africa, the UK and the US), although these policies and measures are mostly general and not specific to synthetic biology. In Canada, a synthetic biology working group is currently exploring ways to gauge the state of synthetic biology research in various sectors, and is examining the feasibility of informal networking/information exchanges between government, industry and academia. Once capacities are identified, research infrastructure development could be pursued through existing policies and programmes such as Networks of Centres of Excellence (NCEs) and government-sponsored public-private R&D entities.

34. In the Czech Republic, the Operational Programme Research and Development for Innovation supports the building of new research infrastructures and /or centres of excellence, e. g. the Biotechnology and Biomedicine Centre of the Academy of Sciences and Charles University in Vestec.[25] A "Roadmap for Large Research, Development and Innovation Infrastructures in the Czech Republic" and funding of research infrastructures is provided by the Ministry of Education, Youth and Sports.[26] The UNIK initiative in Denmark is also supporting research infrastructure development.

35. European Union member countries, such as Germany and Portugal, refer to transnational collaborations that are set up in the frame of the EC e.g. the ERA-NET scheme[27], Joint Programming Initiatives, or the European Strategic Forum for Research Infrastructure (ESFRI).[28]

36. Mexico has supported the development of synthetic biology from research to commercialisation by (i) formulating a national definition of synthetic biology; (ii) launching national research programmes; (iii) supporting the development of an infrastructure for synthetic biology; (iv) developing centres of excellence with new postgraduate programmes; and (v) formulating a clear national bioeconomy objective.

37. In Norway, a Government white paper from 2011 highlighted synthetic biology as an important area for research and future value creation from biotechnology, although no specific measures have been launched to stimulate its development. A Norwegian Network for Industrial Biotechnology has been established as an instrument to stimulate cross-sectoral knowledge transfer, which is likely to cover

23 www.rurdev.usda.gov/BCP_biorefinery.html

24 www.biomassboard.gov/initiative/initiative.html

25 www.opvavpi.cz/, www.biocev.eu/en/

26 www.msmt.cz/vyzkum-a-vyvoj/velke-infrastruktury-vyzkumu

27 http://cordis.europa.eu/coordination/era-net.htm

28 http://ec.europa.eu/research/infrastructures/index_en.cfm?pg=esfri

synthetic biology. However, at present there are very few companies active in this field (the number varies depending on how broadly synthetic biology is defined).

38. As outlined above, the roadmap for synthetic biology in the UK comprises a complete set of policy measures to develop synthetic biology.[29] Government investments include:

- Funding in 2009 of GBP 4.7 million (EUR 5.77 million or USD 3.41 million) for the Centre for Synthetic Biology Research and Innovation (CSynBI) at Imperial College, London, provided by the Engineering and Physical Sciences Research Council (EPSRC);

- The provision of GBP 10 million (EUR 12.27 million or USD 16.89 million) for a national Innovation and Knowledge Centre (known as SynbiCITE), which has leveraged a further GBP 18 million (EUR 22.08 million or USD 30.40 million) from collaborating companies and universities. The centre, at Imperial College, involves 17 universities and 13 industrial partners, including Microsoft, Shell and GSK;

- An investment by BBSRC and EPSRC of GBP 40 million (EUR 49.08 million or USD 67.56 million) was announced in January 2014 to establish synthetic biology multi-disciplinary research centres at Bristol, Nottingham and a Cambridge/Norwich partnership;

- GBP 2 million (EUR 2.45 million or USD 3.38 million) funding from the EPSRC to support Centres for Doctoral Training, with synthetic biology highlighted as a priority area;

- GBP 20 million (EUR 24.54 million or USD 33.78 million) BBSRC funding for six large research projects in synthetic biology. The six projects focus on biotechnology and advanced bioenergy and will use synthetic biology to investigate major global challenges, such as producing low-carbon fuel and reducing the cost of industrial raw materials;

- The Technology Strategy Board (TSB), along with the BBSRC and EPSRC, funds the Synthetic biology Special Interest Group (Synthetic biology-SIG), which is hosted and coordinated by the Biosciences Knowledge Transfer Network. The Synthetic biology-SIG has been set up to help partner the UK's research base expertise in synthetic biology with relevant industrial communities.

39. International collaborations involving the UK include the following:

- The BBSRC is part of the ERASynBio ERA-NET, which has 16 partners from 14 European countries (plus the UK EPSRC and the US NSF as observers). Together they have been working to enhance European and global synthetic biology by structuring and coordinating national efforts and investment, and striving to address a broad range of synthetic biology needs;

- The BBSRC has allocated GBP 6 million in funding for projects that aim to enhance photosynthesis, to be run jointly with the US NSF;

- The BBSRC (along with EPSRC) has provided GBP 1 million (EUR 1.23 million or USD 1.69 million) of funding to the UK arm of the international Sc2.0 project[30], with the aim of building a synthetic yeast genome by 2017; and

[29] www.gov.uk/government/policy-advisory-groups/synthetic-biology-leadership-council

- The BBSRC and EPSRC have provided funding to UK researchers, with matched funding from the Chinese Academy of Sciences (CAS) to Chinese scientists, to partner and develop long-term relationships.

40. In the US, research infrastructure development has had a high priority. Several large universities have established resident synthetic biology centres. UC Berkeley and MIT have one, and the University of Illinois is starting one. SynBERC (Synthetic Biology Engineering Research Center) is a 'virtual' centre of excellence involving multi-university collaboration (Harvard, UC Berkeley, Stanford, MIT, plus some allied universities). Led by bioengineers from UC Berkeley and Stanford University, BIOFAB (International Open Facility Advancing Biotechnology) is the world's first biological design-build facility. This professionally staffed public-benefit facility was founded in December 2009 on the basis of a grant from the NSF. The BIOFAB operates in partnership with the Lawrence Berkeley National Laboratory Synthetic Biology Engineering Research Centre and SynBERC.

41. Department of Energy (DOE) National Laboratories, such as the Lawrence Berkeley National Laboratory (LBNL), also support synthetic biology. The DOE Joint BioEnergy Institute (JBEI) is a partnership led by the LBNL that leverages the scientific expertise, resources, and support of four national laboratories and three academic institutions. In the Fuels Synthesis Division, the JBEI's work in synthetic biology has produced engineered microbes that transform the complex sugars derived from lignocellulosic biomass into biofuels that can directly replace petroleum-based gasoline, diesel, and jet fuel. These advanced biofuels do not require modification of vehicle engines or fuel infrastructures and can be incorporated with no loss of performance. JBEI has produced a portfolio of intellectual property in feedstocks, biomass deconstruction, fuels synthesis, and enabling technologies to help advance the emerging biofuels industry. JBEI is one of three DOE Bioenergy Research Centres (BRCs) established by DOE's Office of Science in 2007 on the basis of a nationwide competition to accelerate fundamental research breakthroughs for the development of advanced, next-generation biofuels.

42. In April 2013, the DOE announced a five-year renewal of funding for JBEI of USD 25 million annually through to 2017. The other two BRCs are the BioEnergy Science Centre (BESC) led by Oak Ridge National Laboratory (ORNL), and the Great Lakes Bioenergy Research Centre (GLBRC) led by the University of Wisconsin-Madison in partnership with Michigan State University. In five years of operation, the three BRCs have produced more than 1 100 peer-reviewed publications and over 400 invention disclosures and/or patent applications.[31]

43. The Defense Advanced Research Projects Agency (DARPA) is developing the Living Foundries: 1 000 Molecules Program, which will result in three new centres (see Box 4).

Scale-up and infrastructure

44. Most countries do not have public-private partnerships (PPPs) focusing on synthetic biology scale-up or infrastructure related to bio-based production. Mexico and the Russian Federation state that they may have such partnerships or infrastructure in the future.

45. Although Canada does not have dedicated PPPs, there are PPPs engaged in general bioeconomy projects and/or bio-based production and health care-related projects. While not specifically directed to synthetic biology, many of these PPPs seek to accomplish innovation-related objectives similar to those that could be achieved through synthetic biology-based projects. They are listed below.

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30 http://syntheticyeast.org/

31 https://newscenter.lbl.gov/2013/04/04/doe-renews-jbei/

- **Networks of Centres of Excellence:** This programme[32] includes the Business-Led Networks of Centres of Excellence (BL-NCEs) and the Centres of Excellence for Commercialisation and Research (CECRs). BL-NCEs are large-scale, not-for-profit collaborative networks led by industry that increase private sector investments in Canadian research. The CECRs are not-for-profit corporations created around academic centres that match clusters of research expertise with the business community.

- **National Research Council (NRC):[33]** The NRC is Canada's federal government agency addressing specific business-identified priorities and challenges by providing: support for small innovative technical and advisory services and research facilities; licensing opportunities; and programmes and partnership opportunities. It also offers incubator services to Canadian businesses through research infrastructure and scientific expertise in a number of fields, including health sciences.

- **The National Research Council-Industrial Research Assistance Programme (NRC-IRAP)**: this programme aims to strengthen business R&D and innovation capacity.[34] NRC-IRAP provides technology assistance to SMEs at all stages of the innovation process and provides linkages to expertise in Canada. A number of small biotechnology firms benefit from this programme.

- **Canada Accelerator and Incubator Program**: Delivered by NRC-IRAP, this programme will provide non-repayable contributions to a limited number of high-potential accelerators and incubators. The selection of incubators/accelerators is currently under review.

- **Genome Canada's Genomic Applications Partnership Program:[35]** Genome Canada is a not-for-profit organisation funded by the Government of Canada to support large-scale genomics public-private innovation focused on key life science sectors. The Genomic Applications Partnership Programme (GAPP) fund collaborative genomics R&D projects between industry and academia.

- **Venture Capital:** To support Canada's venture capital industry, the Government of Canada announced, in January 2013, a comprehensive action plan for deploying the CAD 400 million (USD 370 M) in new capital over the next seven to ten years through the Business Development Bank of Canada (BDC).[36]

46. In the European Union as a whole, no dedicated PPPs with a specific focus on synthetic biology have been created. However, the bio-based industries initiative (BBI)[37] is a major new public-private partnership focused on the bio-based industries in the European Union. The estimated budget of this new initiative is EUR 3.8 billion, of which EUR 1 billion will come from the Horizon 2020 programme budget. The industrial partners (the bio-based industry consortium, BIC) will commit EUR 2.8 billion. The first call for proposals opened on July 09, 2014. Currently there are about 70 private industry partners and over 100 public partners (research institutes and universities). The BBI will focus

32 www.nce-rce.gc.ca/index_eng.asp

33 www.nrc-cnrc.gc.ca/eng/index.html?PHPSESSID=697bb52f80246fabe2c5ea50419c6a1f

34 www.nrc-cnrc.gc.ca/eng/irap/index.html

35 www.genomecanada.ca/en/

36 www.bdc.ca/en/Pages/home.aspx

37 http://biconsortium.eu/about/about-bbi

on higher value-added products. Whether direct or indirect, public-private partnerships are likely to have positive consequences for the synthetic biology community engaged in bio-based production.

47. PPPs exist in the US, but mainly in biofuels production to date. However, the enactment of the five year 2014 Farm Bill, which supports the development of biorefineries in US, gives renewable chemicals and bio-based products parity with advanced biofuels. This means that changes in the construction of biorefineries for renewable chemicals, bio-based products, and advanced biofuels are anticipated. The US Biotechnology Industry Organisation (BIO) and its members are also urging revisions of legislation concerning Production Tax Credits (PTCs), which provide financial support for the development of renewable energy facilities, and Master Limited Partnerships (MLPs), which provide tax breaks for fossil-fuel related activities. The aim in both cases is to extend the schemes to cover the construction of renewable chemicals and advanced biofuels manufacturing facilities.

48. DOE National Laboratories are involved in some PPP's, while the USDA's BioPreferred Program[38] was set up to promote the increased purchase and use of bio-based products. The Energy Biosciences Institute,[39] the largest PPP of its kind in the world and funded for 10 years with USD 500 million (USD 350 million for public institutions), was formed following an international competition launched by the global energy company BP.

49. The UK is the only country reporting PPPs dedicated to synthetic biology. As noted earlier, SyniCITE at Imperial College received GBP 10 million and involves a network of universities and synthetic biology companies. The UK Government, via the BBSRC, has also provided GBP 10 million to the Rainbow Seed Fund, an investment fund specifically aimed at synthetic biology start-ups.[40] In 2012, the Technology Strategy Board (TSB), with co-funding from the BBSRC, ESRC and EPSRC, launched a GBP 6.5 million scheme to provide grants for feasibility studies of innovative industrial applications of synthetic biology.[41] The studies set out to identify commercial opportunities and test feasibility through a programme of experimentation, aiming to acquire new knowledge in order to develop new products or significantly improve existing products, processes or services. Up to GBP 3.8 million was made available in 2014 via the TSB Tools and Services for Synthetic Biology call,[42] with funds coming from the Welsh Government as well as the TSB, BBSRC, EPSRC.

50. The Industrial Biotechnology Leadership Forum was set up to oversee the development of work related to industrial biotechnology, a key technology in the shift to low carbon technologies. Members of the Forum comprise representatives from industry, the Research Councils, TSB, academia, government departments and others.

51. Most countries have policies in place that can be used for scale-up and infrastructure development, although these instruments are mostly generic with few specifically dedicated to synthetic biology development. At a generic level, however, grants, tax incentives, loan guarantees and other instruments designed to facilitate access to venture capital are important, complementary instruments.

52. The US and the UK have complementary policies in place to support scale-up and infrastructure. The UK government recognises the importance of business investment in R&D –

38 www.biopreferred.gov

39 www.energybiosciencesinstitute.org/

40 www.bbsrc.ac.uk/news/research-technologies/2013/131106-pr-synthetic-biology-enterprise-boost.aspx

41 http://bbsrc.ac.uk/news/industrial-biotechnology/2012/120525-pr-government-investment-growth-opp-synthetic-biology.aspx

42 www.innovateuk.org/-/tools-and-services-for-synthetic-biology

particularly by high tech SMEs with a capacity to grow – and provides strong support for this through the R&D Tax Credits scheme,[43] established in 2000. In 2011-2012, this scheme supported an estimated 73% of UK total business R&D revenue expenditure, with nearly 12 200 claims totalling GBP 1.2 billion. The majority of these claims – about 10 100 – were made by SMEs.

53. To allow companies to develop new industrial biotechnology products and technologies, the UK Department for Business Innovation and Skills (BIS) provided GBP 12 million (USD 20 billion) in 2009 for the creation of an open access demonstrator facility in the North East of England, to allow industry, particularly SMEs, access to the expertise and equipment needed to test develop their ideas (see OECD, 2014 and Schieb et al., 2014). The Government also provided GBP 2.5 million (USD 4.2 million) to support companies using the facilities and to match funds from the TSB for new projects related to industrial biotechnology.[44]

54. In the US, various generic instruments, legislative acts and programmes similarly support industry. These include the Advanced Manufacturing Production and Investment Tax Credit, the recent enactment of the Farm Bill; and a Loan Guarantee programme for the construction of advanced manufacturing facilities. Many of these instruments support start-ups and foster collaborations between large and small companies to mitigate risk. The Renewable Fuels Standard (RFS) legislation[45] has proved important in driving innovation in non-biofuel sectors such as renewable chemicals and bio-based products applications.

Intellectual property (IP)

55. There has been speculation that synthetic biology could pose special problems for IP systems, but the evidence suggests that while there could be some unique IP challenges, these are unlikely to be insurmountable.

56. Canada demonstrated concern that the costs to file, prosecute and maintain patents could be very high, amounting to over CAD 150 000 (USD 138 000) per patent family. Concern was also expressed over the possibility of international trade disputes as a consequence of incompatible IPR regimes in different countries

57. The costs of patent filing, prosecution and maintenance are considered major barriers by Canada and Slovenia, with Canada noting that the costs of patent enforcement can easily outweigh the costs of attaining a patent, and that costs such as these can substantially compromise expected returns on investment. The point was also made that the movement toward open science will need to address issues such as reciprocity of intellectual property sharing and how the public and private sectors manage ownership, utilisation and freedom to operate (FTO) issues (see Box 5). As the open science initiative moves beyond enhanced access to scientific publications and towards data sharing and perhaps the sharing of germplasm and molecular tools, a more complex landscape will emerge where conflicting mandates between public and private sector participants will create a need to revisit IP policies and procedures.

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43 www.gov.uk/research-development-tax-credit-smes

44 www.wiltoncentre.com/news/2009/10/16/Investment-supports-pioneering-industrial-biotechnology-work.html

45 www.epa.gov/OTAQ/fuels/renewablefuels/index.htm

58. In the development of synthetic biology for bio-based production, the length of the patent review period was mentioned by Canada and Mexico as a major barrier that could affect efforts to raise venture capital.

59. The Czech Republic referred to the IP issues discussed in the report of the European Academies Science Advisory Council (EASAC) "Realising European Potential in Synthetic biology: Scientific Opportunities and Good Governance".[46] The report discusses the fact that patents should not be too broad, because this may block applications from other researchers. In addition, the report mentions the multi-disciplinary character of synthetic biology and the complexity of products composed of many different parts as major challenges for patenting in this area. However, another line of reasoning points to the fact that, because synthetic biology encompasses entities that are discrete and can be isolated, it is well suited for commodification and the assigning intellectual property.[47] However, Denmark and Germany also mentioned the complex nature of synthetic biology as a possible IP barrier.

60. To support the development of synthetic biology from research to commercialisation, several countries (Canada, Mexico, Slovenia, the UK and the US) mentioned patent clearinghouses (Box 5) as being of major importance or even essential. They are seen as necessary to guarantee access to platform organisms and technologies for the manipulation of genetic material. In addition, open access to data is important to support innovation (Canada, Portugal). The UK recommends streamlining and expanding the boundaries of material transfer agreements (MTAs) to make their use easier and to enhance university-industry flows, noting that freedom to operate (FTO) systems should be made easier and more predictable.

Box 5. Patent clearinghouses and freedom-to-operate (FTO)

In a field such as synthetic biology, in which one engineered microorganism might involve hundreds of different parts and processes and therefore various IPRs and stakeholders, freedom to operate (FTO) may be unclear and therefore hinder innovation. Specific problems include high transaction costs (identification, negotiation and enforcement), legal uncertainty, high royalties and royalties stacking (van Zimmeren et al., 2011). Determining what is already covered by patent rights is a particularly acute problem, but there is some hope that modern text mining and computer-search technologies will help to make analysis of FTO easier and economically more feasible (Rutz, 2009).

The notion arose in the US of an FTO survey, a sort of patent clearance search to confirm compliance with IP law. A clearance survey on the possibility of infringing a third party's patent is traditionally conducted when planning to put commercial projects on the market, but it is frequently conducted much earlier, even at the R&D stage.

In June 2010, the symposium of the National Academy of Sciences and the National Academy of Engineering, "Synthetic Biology for the Next Generation", made recommendations on IP management for the synthetic biology community. One of their recommendations was the creation of clearinghouses. The idea is that a patent clearinghouse, organised by a third party, accepts the registration of synthetic biology inventions, both sequence and functional claims. Typically the functions of the clearinghouse would be:

- To match licensees with licensors;
- To offer standardised licenses;

46 http://www.easac.eu/home/reports-and-statements/detail-view/article/synthetic-bi.html

47 www.easac.eu/fileadmin/PDF_s/reports_statements/Synthetic%20Biology%20report.pdf

- To collect and distribute royalties;
- To enforce patents; and
- To offer dispute resolution via mediation and arbitration.

The incentives for users are safe harbours. Users of synthetic biology inventions though the clearinghouse would be exempted from patent infringement. The incentive for patent owners is assurance of their right to claim royalty fees and lower transaction costs.

Source : OECD (2014)

61. In terms of coping with the shift toward open science and ensuring access to platform organisms and technologies, Canada emphasised the importance of enhanced diligence in establishing legal agreements covering the governance of future relationships. Information system management was also considered to be crucial. To avoid conflicts between proprietary and open relationships, the complexity of contractual obligations should be carefully monitored. In addition, policies surrounding liability, implied warranties and indemnification should be explored and enhanced to mitigate the risk to information providers. Furthermore, access to information for participating nations should be streamlined. Canada believes that longitudinal studies should be undertaken to measure the success of new initiatives, taking into account socio-economic impacts and economic impacts, expanding beyond the traditional indicators used to measure intellectual property successes.

62. Denmark considers that the continuous updating of generic patent legislation would be more beneficial than specific public policies to address IP needs for the development of synthetic biology.

63. Portugal sees a need for better patenting (guidance for good quality patenting); consultancy services to encourage mediation between scientists and patent offices and lawyers; new business models for patent licensing, such as clearinghouses and clearing pools; and funding of multi-disciplinary technology transfer teams in academia (technology transfer offices, TTOs) to simplify the transfer of knowledge and technology.

64. South Africa pointed to the need for harmonisation of plant breeders' rights (PBR), patents, and its national IPR-PFRD act (Intellectual Property Rights from Publicly Financed Research and Development Act). Consideration of the wider issues involved in harmonising regulations and strategies relevant to the promotion of biotechnology and synthetic biology in the country was considered desirable.

Demand-side aspects

65. To improve the uptake of synthetic biology derived bio-based products, most countries agree the importance of certification and labelling initiatives (Belgium, Canada, Denmark, Italy, Mexico, Norway, Portugal, South Africa and the UK) and public procurement initiatives (Canada, the Czech Republic, Denmark, Italy, Mexico, Portugal, South Africa, Slovenia, the UK and the US), often pursued in combination. Other initiatives, including specific market-readying initiatives, are considered important by six countries (Canada, Denmark, the Russian Federation, South Africa, the UK and the US).

66. Several countries (Belgium, Canada, Portugal and the UK) concur that regulatory issues and biosafety regulations are of major importance when supporting the uptake of synthetic biology derived bio-based products.

Public opinion and engagement

67. Although most countries pointed to the importance of public education, only South Africa and the UK include communication as an integral part of the strategy for synthetic biology. The UK argues that public acceptability and environmental impact are key issues that may act as barriers to research and the commercial deployment of synthetic biology. This is similar to the way that GM has been affected to date. Advances in synthetic biology give rise to a host of questions concerning ethics, social justice and bio-security. The UK government's stated policy of transparency and openness concerning synthetic biology is reflected by the publishing of policy developments on the government's website.[48]

68. The Research Council of Norway is in the process of developing a framework for responsible research and innovation (RRI) for the development and deployment of emergent technologies.

69. The US identified a need for regulatory clarity to address possible effects of the environmental release of products or applications from synthetic biology. Public policy and public perception issues are very often solely based on the anticipated negative effects of gene modification technology. Public policy should address regulatory issues so that the investments in fundamental and translational research contribute to beneficial applications and products for society. Public education and outreach should also address the benefits of synthetic biology – especially in everyday products.

70. Nevertheless, the US does not have a universal national strategy for communication on synthetic biology. There are many elements, however, that can be incorporated into good communication practice, such as the educational materials of BIO's Synthetic Biology Working Group;[49] the Woodrow Wilson Centre's synthetic biology inventory;[50] and education materials from the SynBERC's ERC. The FBI is developing measures to educate synthetic biology practitioners about the security aspects of their work, and it has also sponsored a biosecurity prize at the iGEM competition.

Overall commercial impact

71. The final question in the survey asked what countries considered to be the three most useful things that could be put in place in the country to help accelerate the delivery of commercial impact from synthetic biology. The responses can be summarised as follows:

- Stimulation of synthetic biology research in dedicated centres of excellence, with dedicated programmes linked to the development of the bio-economy;
- Ensuring that legislation and regulation enable the uptake of products developed through synthetic biology, including safety regulation and IP issues;
- Communication with the public and educational efforts to make synthetic biology understandable and highlight potential benefits; and

48 www.gov.uk/government/policy-advisory-groups/synthetic-biology-leadership-council

49 www.bio.org/category/synthetic-biology

50 www.synbioproject.org

- Incentives for existing companies and start-ups to engage in technology transfer and commercialisation activities.

Table 4. An overview of answers regarding the most useful future developments.

Q19: What are the three most useful things that could be put in place in your country to help accelerate delivery of commercial impact from synthetic biology?	
BE	1. Develop policy for research and innovation in synthetic biology e.g. support for inter-disciplinary research between strategic research centres (VIB, imec, iMinds)[51]. 2. Put biosafety regulation in place without hindering innovation. 3. Increase public understanding for benefits and risks.
CA Defense R&D Canada	1. Increased support for advanced development (funding and support by government laboratories). 2. Increased research funds. 3. Government funded core facilities for manufacture and scale-up.
CA, Strategic Policy Branch, Health Canada	1. A coordinated value chain that works at developing products for a market that is ready to accept the technology (note: as with GE crops, the Government of Canada's role in establishing market cohesion is limited to supporting forums/moderation). 2. Regulatory harmonisation at the domestic level, and with key international markets. The concept of novelty used in Canada is an example of how existing regulation that would be beneficial as products of synthetic biology would likely be evaluated in the same manner as other novel products i.e. evaluating the novel product *versus* the process through which it was created. 3. Ensure the public is engaged and well-informed about the rigours of the regulatory system to provide reassurance of the safety of products of synthetic biology. 4. Increased investment in synthetic biology, from foundational research and development (including platform technologies), translation of basic research to ventures, and development of a coordinated value chain that develops products for a market that is ready to accept the technology. 5. Development of public/private partnerships for synthetic biology.
CH	1. A NCCR (National Centres of Competence in Research) programme. 2. Solid technology transfer for such a NCCR. 3. Early involvement of companies.
CZ	1. Targeted support to education, research and development in synthetic biology. 2. Investing in interdisciplinary research to generate synergies. 3. Promoting strategic PPPs, involvement of industry, fast knowledge transfer.

[51] VIB, Flanders Institute for Biotechnology ; imec, Interuniversity Centre for Nano- and Micro-electronics; iMinds, digital research centre and business incubator

DK	1. A general support to initiatives enabling the bio-based society. 2. Securing strong academic groups covering a broad suite of technologies (e.g. fermentation process development, molecular biology, metabolic engineering and chemistry). 3. Make sure that current and future legislation support fast production and product approval of products developed by synthetic biology. A dedicated synthetic biology approval system would most likely just slow bureaucratic procedures down without providing better safety for the environment and consumers.
DE	1. R&D efforts should concentrate on applications that are accepted by the broader public. 2. Create public acceptance through transparency and education. Avoid negative public reactions because of ignorance. 3. Strategic guidance for responsible research.
IT	1. Support R&D for pre-competitive research. 2. Simple adoption of existing public (for example: UK) or private (for example, Novo Nordisk Foundation Centre for Biosustainability) roadmaps. 3. Support public engagement.
MX *	1. Declare a national programme on synthetic biology as support for a bioeconomy. 2. Dedicated centres, research and innovation programmes to boost applied projects on synthetic biology. 3. Incentives and initiatives for start-ups based on synthetic biology and those companies that develop innovation business based on synthetic biology.
MX **	1. R&D funding. 2. Tax incentives for companies that employ synthetic biology-derived technology. 3. Provide scholarships for Mexican students to have research stays at laboratories that are leaders in the field of synthetic biology.
NO	Provide clear-cut criteria for safety approval.
PT	Support (funding) of the close to market projects (incentives to SMEs, if any…) and public opinion education
RU	System measures for industry development.
SI	1. Increased financial support for start-up companies. 2. Increased funding for basic research projects in synthetic biology. 3. More effective technology transfer offices.
UK	1. Effective networking between research and commercial undertakings based on current investment in synthetic biology research centres, CSynBi and SynbiCITE. 2. Appropriate regulatory framework that promotes responsible innovation and commercialisation. 3. Development of an internationally agreed treatment of standards and IP.
US	1. Coordinated federal government approaches based on synthetic biology to foundational and translational research, which result in loan guarantees, grants, and tax incentives for advanced manufacturing facilities. 2. Explore novel PPPs for company adoption in a product development pipeline. 3. Regulatory / public policy work anticipatory of the needs / impacts. 4. Public education and outreach demonstrating the benefits of synthetic biology.
ZA	1. Broader understanding of the relevance for synthetic biology in a bioeconomy. 2. Complementary regulations/legislation that enable its use. 3. Support for research, development and innovation.

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Conclusions

Definition of synthetic biology

72. Very few countries have an official definition of synthetic biology. The field is advancing very rapidly, and the challenge is in providing a definition that is;

- Of practical value (e.g. to research councils, regulators); and
- Sufficiently broad to allow for further developments in the field (i.e. to keep it relevant in the future).

73. For governments, the most useful type of definition is likely to be an operational definition, focused on actual activities, applications and products of synthetic biology rather than on abstract concepts and metaphors. The OECD definition of biotechnology may serve as a model in developing such a definition for synthetic biology.

Coordination of policies to avoid policy conflicts and disconnects

74. Under the over-arching umbrella of a focus on green growth, many countries are evolving bioeconomy strategies, with marked commonalities and differences across countries. Also noticeable are attempts to evolve specific plans and roadmaps for the development of industrial biotechnology, and in some instances there are dedicated attempts to exploit the potential of synthetic biotechnology in bio-production processes.

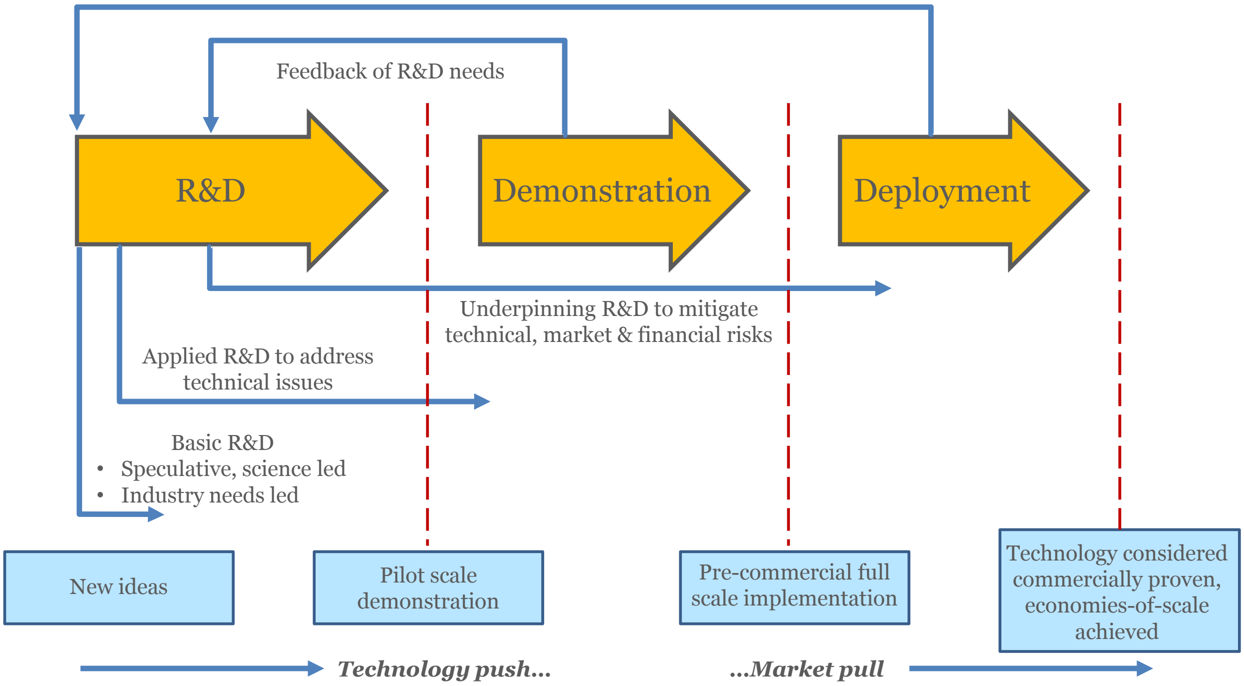
75. It is clear, however, that these policy thrusts are not always closely aligned. For example, although ten out of seventeen identified public funding for synthetic biology R&D that focused on applications to develop and produce bio-based products, only four countries in this survey envisaged bio-based production using synthetic biology.

76. Ensuring the close alignment of strategies concerning the development and use of synthetic biotechnology, the growth of industrial biotechnology and the evolution of a bioeconomy will be important if the full potential of synthetic biotechnology is to be realised and significant conflicts avoided at the intersection of bioeconomy strategies with broader policy spheres spanning industry, the economy, agriculture, the environment and health.

Scale-up and infrastructure

77. As a reminder of the scale of investment needed, perhaps it is worth reflecting on the innovation chain (Figure 3). Public policy often focuses on the R&D phase, and yet of all the stages involved in the bio-based production cycle or chain, scale-up is usually the most difficult and expensive. Several of the earliest synthetic biology/biofuels companies in the US ran into major difficulties when attempting scale-up.

Figure 3. The generic innovation chain.



78. In this survey, only four countries say that they are funding scale-up projects relating to synthetic biology. This means that either scale-up is being left to private industry or it is not happening at all. Scale-up is vital if a country is to capitalise on domestic R&D. Otherwise, capacity building in the industry will happen in other regions. This has been often been a common complaint in Europe.

79. The general message is that OECD countries adept at synthetic biology research are likely to lose out in terms of job creation and value-added unless policies covering the whole value chain are developed in an integrated fashion

80. Bearing all this in mind, particular attention should be paid to Table 4 (see earlier). Even though countries are at different stages of development and the policy steps they see as most useful and advantageous to take in their own contexts may not be applicable to all, there is still considerable scope for countries to learn from each other.

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ANNEX 1: SURVEY: FUTURE POTENTIAL OF SYNTHETIC BIOLOGY IN BIO-BASED PRODUCTION

Purpose

Overall, the survey is designed to show to what extent synthetic biology is considered an inherent part of bioeconomy strategies, and how countries are tackling the policy issues being created by synthetic biology.

Scope

The future potential of synthetic biology in bio-based production in any country depends on several critical factors:

- An aspiration towards the development of a bioeconomy with bio-based production as a central role to play;
- The availability of R&D support (for pre-competitive research);
- Support for post-proof-of-concept R&D e.g. demonstrator plant design and construction;
- A strategy for scale-up and infrastructure development, which will probably rely on public-private partnerships (PPPs);
- The future direction of intellectual property in the life sciences, and some specific matters associated with synthetic biology;
- Attention to demand-side aspects, such as readying markets for these new products, public procurement;
- Careful attention to public engagement.

The survey is designed to discover, at the country level:

- If there is as an awareness of synthetic biology in bioeconomy strategies, and also if bioeconomy strategies are coordinated with synthetic biology roadmaps;
- What policy measures are being used that are critical to the development of synthetic biology e.g. R&D support, intellectual property, public engagement.

Guidelines

Responses to the questionnaire should be provided electronically by first saving the form on your computer desktop and then emailing the completed form as a Word attachment. Please send completed questionnaires electronically to the following contacts at the OECD WPB Secretariat:

Mr Jim Philp, OECD
Email: james.philp@oecd.org
Tel: 00 33(0) 14 5 24 91 43

Ms Kathleen D'Hondt
Email: Kathleen.Dhondt@oecd.org
Tel: 00 33(0) 1 45 24 98 12

Note: Double clicking on a check box should bring up a Check Box Form Field Options box. The default value is “Not checked”. If you wish to check the box, select the second option, “Checked”.

REQUEST FOR INFORMATION

Contact details of the primary contact person in the responding country

Country:

Your name:

Your organisation:

Your position:

Your area of responsibility:

Telephone number:

E-mail address:

The questionnaire should be returned by 14 February 2014 and please refer to “WPB Synthetic biology” in the subject field of your e-mail. In case of any further questions, please do not hesitate to contact the Secretariat (details above).

<u>Bioeconomy and synthetic biology</u>

Q1: Does your country have an official definition of synthetic biology ?

Q2: If yes (to Q1), what is it, and can it be found in a document on the web ?

Q3: Does your country have, or is it developing, a bioeconomy strategy ?

Q4: If yes (to Q3), does this bioeconomy strategy envisage bio-based production using techniques of synthetic biology ?

<u>Synthetic biology roadmaps</u>

Q5: Does your country have, or is it developing, a roadmap for synthetic biology?

Q6: If yes (to Q5), does it include envisaged applications of synthetic biology (choose from the list):

☐ Agriculture (crops/feedstocks)

☐ Bioenergy (principally transport fuels)

☐ Biomedicine/ health/ pharmaceutical

☐ Environmental (e.g. bioremediation of contaminated land and water, wastewater treatment)

☐ Biosensors

☐ Chemistry (bulk and fine)

☐ Plastics

☐ Marine applications

☐ Others (please specify)

<u>R&D support for synthetic biology</u>

Q7: Does your country, through its national or regional research councils (or their equivalent), have dedicated calls for research proposals for synthetic biology?

Q8: If not (to Q7), how is synthetic biology research funded in your country?

Q9: Is public funding for R&D in synthetic biology in your country focused on:

☐ Basic science

☐ Enabling technologies (e.g. gene synthesis technologies, error control, software development)

☐ Applications of synthetic biology related to bio-based production (e.g. bio-based fuels, chemicals, plastics, materials)

☐ Scale-up (e.g. biomanufacturing technologies, demonstrator plants)

☐ A mixture (please specify).

Q10: What policies are being used to support research infrastructure development? (e.g. international collaborations, setting up research centres of excellence, knowledge transfer networks, both physical and internet).

Scale-up and infrastructure

Q11: Does your country have public-private partnerships (PPPs) whose focus is on synthetic biology scale-up or infrastructure related to bio-based production ? (In this context, scale-up could refer to demonstrator plant or full-scale plant construction, and infrastructure is taken to mean manufacturing infrastructure, rather than research).

Q12: What public policies areas are most appropriate to scale-up and infrastructure development ? (e.g. advanced manufacturing tax credits, R&D tax credits, loan guarantees).

Intellectual property (IP)

Q13: What, broadly, are the most significant IP barriers to the development of synthetic biology for bio-based production ? (e.g. review period at national Patent Offices, barriers to open innovation).

Q14: What are the most significant IP developments that will enable the development of synthetic biology from research to commercialisation ? (e.g. clearinghouses).

Q15: What public policies would best enable the developments in Q14 ?

Demand-side aspects

Q16: What can governments do to improve uptake of synthetic biology-derived bio-based products ?

☐ Support certification and labelling initiatives

☐ Public procurement programmes

☐ Specific market readying initiatives (please specify)

☐ Other (please specify)

<u>Public opinion and engagement</u>

Q17: Does your country have a strategy for public dialogue on synthetic biology?

Q18: If yes (to Q17), what is being done in your country regarding public engagement in synthetic biology ?

<u>Overall commercial impact</u>

Q19: What are the three most useful things that could be put in place in your country to help accelerate delivery of commercial impact from synthetic biology?

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE