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Synthetic Biology
From Science to Governance

A workshop organised by the European Commission's Directorate-General for Health & Consumers

18-19 March 2010, Brussels

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Introductory note

We live in times of change. Economic, social, cultural, as well as technological change. Some of the technological change may come through revolutionary sciences like the new field of Synthetic Biology.

Synthetic Biology is an exciting area of research. It contributes to a paradigm shift in biology by importing conceptual models from informatics and engineering and breaking down traditional disciplinary barriers. Concretely, "SynBio," as it is often nicknamed, promises a wide variety of applications driven, in particular, by the need for "cleaner" and more efficient chemical manufacturing, "cleaner" energy, environmental technologies, and new medicines.

Innovation must not only satisfy needs but also meet basic safety requirements. Therefore, Synthetic Biology should combine innovative solutions with inherently safe design. To take a metaphor often used by Synthetic Biologists to explain their engineering approach to biology, namely car manufacturing, safety has become an integral part of car design. It is not an option, an add-on or an afterthought. Nowadays, who would want a car that could be, as Ralph Nader put it in his time, "unsafe at any speed"?

The European Commission has been and will continue to be an enthusiastic promoter of innovation and progress aiming to improve citizens' life. With funding pioneering research, supporting collaboration and promoting innovative ideas, we stand behind the efforts of bright scientific teams and entrepreneurs in Europe and abroad.

This workshop takes us one step forward in strengthening our efforts towards developing a robust, responsible, and safety-conscious Synthetic Biology community in Europe and abroad.

Paola Testori-Coggi
Director General
European Commission, Health and Consumers Directorate General

Executive Summary

On 18-19 March 2010, the European Commission's Directorate General for Health and Consumers (DG SANCO) organised a workshop in Brussels on synthetic biology (SynBio) – an exciting and rapidly developing area of research with many promising applications.

The aims of the workshop were two-fold:

- to provide an overview of the science and its applications, from those that are ready to be marketed today to those that remain at the conceptual stage
- to discuss the challenges and opportunities of SynBio in terms of governance, social, ethical and legal issues

This report on the proceedings of the workshop provides a non-exhaustive overview of the discussions that took place over the two days. It is divided into four sections:

- A summary of the opening keynote speech by Professor Richard Kitney on the defining characteristics of SynBio, the factors driving its development, different approaches to the science, the prospects for its evolution and key factors for its future success; as well as a snapshot of the European SynBio research community
- An overview of work underway or in prospect on SynBio applications in three key areas: energy, the environment and health
- Views on the implications of SynBio in terms of: ethics; governance; security implications; risk assessment and management; public opinion; and patenting issues
- Preliminary conclusions from the workshop

SynBio is an emerging field of science made up of different but overlapping strands, distinct from but linked to more established fields such as biotechnology and systems biology. It has the potential to influence, or even transform, a range of areas of our economy and society. Yet because SynBio is so new, it remains, in a very real sense, still to be defined – both in terms of its boundaries and its implications for regulators.

This two-day workshop marked an important step in the European Commission's attempts to assess just what those implications are. The information presented and the views exchanged are a contribution to the process of assessing whether the specificities of SynBio are such that it demands a specific regulatory framework at EU level, and what form that framework might take.

Synthetic Biology – where we are and where we are heading

The opening address of the workshop was given by Richard Kitney, Chairman of the Institute of Systems and Synthetic Biology at Imperial College, London. Kitney offered two complementary definitions for SynBio: 'designing and making biological parts and systems that do not exist in the natural world using engineering principles' and 'redesigning existing biological systems, again using engineering principles'.

Several factors have spurred the development of SynBio: advances in high-speed DNA sequencing and DNA synthesis; the development of powerful computers; the growth of the internet; and the rollout of broadband networks. These have facilitated the confluence of biology, engineering and physical science, which has perhaps been the most significant factor behind the emergence of SynBio.

A key distinction between SynBio and Systems Biology, said Kitney, is that whereas the endpoint of analysing biological systems is Systems Biology itself, the endpoint of SynBio is industrialisation. SynBio is a broad church not only in the sense that it combines fundamental scientific disciplines such as bio-nanotechnology, synthetic genomics and engineering, but also in that it integrates social science and ethics into the field.

In scientific terms, Kitney argued, there are four approaches to SynBio:

- Bottom-up: for instance, constructing synthetic genomes by assembling chemically synthesised oligonucleotides, joining them *in vitro* to produce intermediate assemblies and then cloning them
- Metabolic engineering: the classic example of this being the production of the anti-malaria drug Artemisinin through the synthesis of the eponymous substance found in the plant *Artemisia annua*
- Chassis: the creation of fit-for-purpose chassis based on naturally occurring ones such as E. Coli or B. Subtilis
- Parts, devices and systems: the development of systems based on devices comprising standard parts, as in the world of engineering

This fourth approach to SynBio translates as parts encoding biological functions (such as modified DNA); devices made from a collection of parts and encoding human-defined functions; and systems that perform specific tasks.

In terms of the evolution of industrial approaches, SynBio may well follow the route taken by the computer industry in the 1980s. Many companies began with a vertically integrated model, active in all areas of the value chain – components, product design, assembly, operating systems, applications software, sales and distribution and field service. Over the years, they became far more specialised, forging partnerships with companies operating in distinct areas. A similar pattern is occurring in biotechnology and can be expected to occur in SynBio too. A decade ago, companies like Dow, DuPont and Monsanto were active throughout the biotechnology value chain, from design and simulation through to sales. Since then, they have become more specialised, while new players have chosen to be more focused from the outset.

If this process were to be emulated in the case of SynBio, there would be three key phases in the value chain involving distinct actors:

- *Specification, design, modelling, implementation, testing and validation:* universities working in partnership with appropriate companies
- *Assembly of parts and devices:* carried out in-house in university research laboratories or by gene synthesis companies, depending on the scale
- *Applications:* implemented by companies e.g. in the healthcare, pharmaceuticals, biofuels or agro-science sectors

Kitney also argued strongly that there exist three prerequisites for facilitating and accelerating the transition of SynBio from the research laboratory to industrial applications:

- A professional registry of parts provided by universities and other research organisations and taken up by industrial and other users
- A common set of standards for parts, which will be as important for SynBio as it is for other industrial sectors based on the engineering of complex systems
- A registry of standard models to enable the prediction of complex systems' behaviour

The potential implications of SynBio for humanity could be so immense, Kitney concluded, that we may be on the cusp of a new age in scientific development – the biological age, following on from the analogue age and the digital age. SynBio promises to have an impact on the economy comparable to that of information and communications technologies over the past three decades, with biofuels, biomaterials, medicines and biosensors among the areas likely to be at the forefront of this 'new industrial revolution'.

SynBio and EU research

For Ioannis Economidis of the European Commission's Directorate General (DG) for Research, SynBio offers a new conceptual framework, which:

- addresses biological systems with the tools and the descriptive language of engineering
- tackles old questions and challenges with fresh approaches inspired by electrical circuitry and mechanical manufacturing, and
- pursues the creation of new materials with *à la carte* properties based on the rational combination of standardised biological parts decoupled from their natural context

Economidis briefly outlined some of the 18 projects that were selected for funding under the European Commission's Sixth Framework Programme, and specifically the NEST PATHFINDER initiative on SynBio, launched in 2003. These include application-specific work in areas ranging from energy to healthcare, as well as horizontal projects looking at SynBio from a European perspective and analysing the safety and ethics of synthetic life.

SynBio research is also taking place in the context of the EU-funded Knowledge-Based Bio-Economy (KBBE) programme, which aims to help transform life sciences into new, sustainable, eco-efficient and competitive products. The term 'bio-economy' covers all industries and economic sectors that produce, manage and otherwise exploit biological resources, Economidis explained. These include agriculture, forestry, food and fisheries.

Finally, Economidis drew attention to the existence of an ERA-NET (European Research Area Network) for SynBio. The aim of this, he said, was to provide the basis for a successful forum for the exchange of information between EU member states; to begin identifying research complementarities and to set up future joint transnational calls.

The European SynBio community

Where in Europe are the greatest concentrations of SynBio researchers to be found? Thomas Reiss of the Fraunhofer Institute for Systems and Innovation Research in Karlsruhe presented the results of a study into the distribution of the European SynBio community. The study was carried out by TESSY (Towards a European Strategy for Synthetic Biology), an EU-funded project for which the Fraunhofer Institute is the coordinating partner.

In 2007-2008, said Neiss, the largest number of identified SynBio experts was in the UK (around 190), followed by Germany (around 105), Spain (80), Switzerland and France (around 40 each). Approximately 90 percent of the European SynBio community work in research institutions (of which 69 percent are based in universities and 31 percent in other public research bodies). Strikingly, only 7 percent of SynBio researchers are based in industry, with the majority of them working for SMEs.

Highlighting the interdisciplinary nature of the community, Reiss said 37 percent of SynBio researchers had a background in biology, 14 percent in chemistry, 12 percent in informatics and 10 percent in engineering. The remainder came from a broad range of disciplines, including physics, environmental sciences, medicine, social sciences and energy technologies.

Reiss presented some of the key features of TESSY's 'SynBio roadmap for Europe', an exercise which sought to set out milestones for SynBio's development up to 2016. In addition to the science of SynBio, the roadmap also addressed forthcoming challenges in terms of knowledge transfer, funding and regulation. Progress in one of these fields would depend on advances in others, he said, adding that public support and understanding of SynBio research were key to enabling funding and regulation to sustain significant scientific steps forward.

Academic and industrial research perspectives

Prospects for SynBio applications

Hubert Bernauer of the International Association Synthetic Biology introduced the issue of SynBio applications with a citation from Martin Fussenegger: "The field has had its hype phase. Now it needs to deliver!"

The technology-driven phase of SynBio's development is now running in parallel to a market-driven phase, said Bernauer; the SynBio community will soon need to start delivering innovative products in order to increase awareness of the importance of the science.

SynBio now finds itself caught between the scientists' urge to push the boundaries of knowledge and the pragmatism of investors who want to know the practical benefits of the technology for consumers, the costs and the timeline for a return on investment. Yet as Bernauer argued, in the third phase of SynBio – the development of primary gene products – we are already seeing the emergence of marketable uses for the technology, for instance in leather processing, the cleaning industry and in the field of diagnostics.

The potential markets for SynBio applications, said Bernauer, were the same as for biotechnology more broadly, with applications likely to emerge first of all predominantly in the medical/pharmaceutical field and next in the industrial field (respectively known as red and white biotechnology).

SynBio seen from Genopole, France

Hubert Bernauer's intervention was followed by a brief presentation by Françoise Russo-Marie of Genopole, the biopark at Evry, 35km south of Paris, which was established in 1998. As Russo-Marie explained, Genopole was created to promote research in genetics, genomics and post-genomics; and to implement a 'technopole' fostering the creation and development of biotechnology companies.

The growth of the biopark since its establishment has been exponential – by 2008, it hosted 69 biotech companies, 20 academic labs and 19 large-scale facilities. The direct head count had reached 2,293, with up to 6,000 jobs generated indirectly. An Institute for Systems and Synthetic Biology was opened in 2009, though Genopole has run a research network on SynBio since around 2005. Research is focused on genome design, bioproduction, bioenergy, regulatory networks, metabolic networks and developmental biology.

Energy applications

Boosting energy crop yields

A perspective on SynBio applications in the energy field was provided by Paul Willems, Associate Director of the Energy Biosciences Institute (EBI) at the University of California, Berkeley, as well as Technology Vice President at BP.

When it comes to developing transport fuels or other energy applications using SynBio, the aim must be for these to be economically viable. Their diffusion must not be reliant on subsidies or driven by specific policy incentives, Willems argued. Rather, the intention must be for consumers to be attracted to SynBio products

because they are cheaper than their traditional counterparts. As such, the emphasis in the energy industry is on developing new manufacturing routes and improving existing pathways and organisms rather than starting from scratch.

The EBI is a multidisciplinary institute, bringing engineers, biologists, chemists and economists under one roof and facilitating interaction between academia and the corporate world. It carries out both open and proprietary work, with around 90 percent of current activity focused on lignocellulosics and the development of second and third generation biofuels. The EBI's research priorities are:

- To develop energy crops and associated agronomic practices
- To identify or create more active catalysts for the conversion of biomass to sugars and sugars to fuels
- To develop improved industrial micro-organisms
- To develop new types of micro-organisms that produce and secrete hydrophobic compounds
- To understand the social, economic and environmental implications

Willems highlighted the differences in yield growth over the past century in crops that have been heavily invested in, such as corn, to show the potential of modern biological, agronomical and breeding techniques for increasing productivity. The energy grasses that are now the object of attention at EBI should be able to demonstrate a similarly striking improvement in yields in a much shorter timeframe, thanks to modern biological techniques and the improved data set now available.

The key challenges in conversion research are: to overcome the recalcitrance of lignocellulosic biomass (if plants and trees stand straight it is because these materials have evolved so as not to degrade easily); to increase efficiency in the utilisation of sugars; to produce better fuel molecules beyond ethanol; and to create a highly productive and stable host organism.

Cleaner biodiesel

There followed a presentation by Joel Cherry, Senior Vice President for Research Programs and Operations at Amyris in San Francisco, of the company's activities in the development of renewable fuels.

Using a platform developed for the production of the anti-malaria drug Artemisinin (see below), Amyris is working on the production of bio-derived diesel and jet fuel from the conversion of sugar cane using genetically engineered yeast. Amyris' diesel-fuel product has been registered with the US Environmental Protection Agency at a 20 percent blend and the company hopes that a 35 percent blend will be approved in the near future. The product meets all of the regulatory requirements for a diesel fuel and is comparable in energy density to a traditional diesel, and better in terms of having a lower cloud point and a higher Cetane number, said Cherry.

Among the other environmental benefits of this diesel (when produced from Brazilian sugar cane) are: zero sulphur emissions, a 90 percent reduction in greenhouse gas emissions, and significantly lower emissions of Nitrogen oxides and particulates than other available biodiesels. Amyris is aiming to begin commercial production of its diesel and chemical products by 2011 and is

predicting annual output of 450 billion gallons (1,703 billion litres) of diesel and 124 billion gallons (469 billion litres) of jet fuel by 2020.

Environmental applications

Biodegrading chemicals through genetically engineered bacteria

A brief overview of the potential for environmental applications of SynBio was given by Victor de Lorenzo of the Centro Nacional de Biotecnología in Madrid (CNB). There are four main areas of application for engineered biological agents in the environmental field:

- bio-transformation, or increasing cells' production of certain substances
- detection of environmental contaminants and pathogens
- immobilisation of distinct chemicals
- *in situ* biodegradation

In the first three areas, the last twenty years have seen great leaps forward thanks to classical genetic engineering techniques. However, this has not been the cases for *in situ* biodegradation. Efforts to create superbugs capable of biodegrading toxic or hazardous substances have met with far more limited success.

It is therefore in this area of environmental application that the potential of SynBio could be greatest, according to de Lorenzo: by deep genomic engineering of bacteria capable of biodegrading chemicals either in cases of accidental release or for applications in industrial treatment plants.

Health applications

Synthesising Artemisinin

The best-known SynBio health application to date is probably the production of Artemisinin. The drug, used to treat multi-drug resistant strains of falciparum malaria, is derived from artemisinic acid found in the plant *artemisia annua*, also known as sweet wormwood. Around 600 million tonnes of this plant are grown each year, but due to the time it takes to grow them to maturity (two years), global Artemisinin supply suffers from cyclical gluts and drops.

As Joel Cherry explained, with the help of a $20 million grant from the Bill and Melinda Gates Foundation, Amyris has developed a process for synthesising Artemisinin in just two weeks. The process involves a multi-step enzymatic conversion of sugar cane into artemisinic acid, which can then be converted chemically into Artemisinin. In April 2008, Amyris announced a partnership with Sanofi-Aventis for the large-scale production of synthesised Artemisinin.

SynBio and biopharmaceuticals manufacturing

Sven Panke of the Department of Biosystems Science and Engineering at ETH Zurich focused on SynBio's potential for rendering the production of drugs easier.

The emerging discipline offers a unique opportunity to remove some of the major existing bottlenecks in biopharmaceuticals manufacturing, Panke argued. These bottlenecks include microheterogeneity in proteins, secretion and folding.

SynBio introduces four key new strategies for dealing with these problems, Panke said: parallel, orthogonal metabolisms; drastically increased design power at all levels of the design process; simplified, reduced chassis; and molecular building blocks.

Probiotics, tumour-fighting and cholesterol-ingesting bacteria

Vitor Martins dos Santos, Chair for Systems and Synthetics Biology at Wageningen University in the Netherlands, discussed a number of potential applications for SynBio in the sphere of food and health. These include:

- more efficient production of 'nutraceuticals' (such as vitamins, food supplements and preservatives) and probiotics (dietary supplements of live micro-organisms thought to be healthy for the host organism)
- reprogramming stem cells
- regenerative medicine
- alternative processes of drug production
- new therapeutic methods (including de novo designed vaccines)
- non-invasive diagnostics
- engineering human immune cell responses (providing defences against cancer, inflammation, or auto-immune diseases)

Martins dos Santos also highlighted the possibility of reprogramming host-pathogen interactions and, in a longer-term perspective, the prospect of developing bacteria that could be injected into organisms to seek out and attack tumours (as already tested in mice).

Pawan Dhar, who recently left RIKEN, Japan to set up Centre for Systems and Synthetic Biology at the University of Kerala in India, informed of the work of Takuya Ueda and Yoshihiro Shimizu of Tokyo University who are working on designing bacteria that ingest cholesterol, with obvious potential benefits for patients with high cholesterol in their blood.

Developing new molecules, drugs, combating drug resistance

Pawan Dhar presented potentially groundbreaking work on making 'proteins from non-coding regions'. His research showed that transcriptionally unused regions of the E.coli genome could be artificially expressed to make novel proteins, leading to interesting applications. Of the seven artificially produced proteins in his lab, two of them slow down the cell growth and show evidence of tertiary structure. This could lead to the emergence of, what he calls, 'combinatorial genomics'.

Wilfried Weber of the Centre for Biological Signalling Studies at the University of Freiburg, Germany outlined other opportunities offered by SynBio in terms of the discovery and development of new drugs. SynBio, he said, enables us to better understand the molecular basis of disease. This has already allowed us to:

- identify the molecular basis of a rare form of agammaglobulinemia, a genetic disorder which affects the body's ability to fight infection
- trace back the SARS (Severe Acute Respiratory Syndrome) epidemic pathway to understand how the disease was transferred from bats to humans
- understand the virulence of the influenza virus, by reconstructing close relatives of the Spanish flu virus which killed 50-100 million people in 1918

An example given of a Synbio-based biopharmaceutical was a polio vaccine produced by synthesising a poliovirus genome. This has shown to be effective in mice and is very likely to be applicable to the attenuation of other viruses. Weber also presented work underway using SynBio techniques to find ways to shut off antibiotic resistance in tuberculosis.

SynBio also offers solutions to infestations of disease-transmitting insects. Male insects can be released which carry a female-specific lethality determinant, so that when they mate with females in the wild they will produce no female progeny. The release of a synthetic gene switch for inducible female-specific lethality was approved by the US Department of Agriculture in May 2009.

The final example of SynBio-based biopharmaceutical applications presented was that of smart drug deposits. Patients requiring frequent intravenous administration of drugs can suffer from pain in the injection spot. A solution can be provided through implantable 'smart drug depots' that release a defined drug dose in response to an inducer molecule that can be administered orally.

Outlook

Weber concluded with an overview of the outlook for SynBio in drug discovery. SynBio provides new insights into disease mechanisms, facilitates the discovery of conventional small molecule compounds and enables the design of biopharmaceuticals with unprecedented functionality and safety, to treat and prevent diseases and to overcome drug resistance.

However, said Weber, the potential of SynBio in drug discovery would only be fulfilled by supporting research in universities and SMEs, where most innovation is currently underway. This is necessary not only in order to stimulate entrepreneurship but also because so much SynBio research is directed at diseases prevalent in developing countries, which traditionally face more of a struggle to attract funding from major drug companies.

Ethics and Governance

Ethical issues

Göran Hermerén, Professor of Medical Ethics at Lund University and President of the European Group on Ethics in Science and New Technologies (EGE) presented the key issues and challenges in developing an ethical framework for SynBio. The EGE was asked in May 2008 by European Commission President José Manuel Barroso to prepare an opinion on the 'ethical, legal and social implications' of SynBio. This opinion was published in November 2009.

The convergence of emerging technologies, including infotech, biotech and nanotech, may lead to radical changes in our lives and create different ethical and societal problems from those raised by any of these technologies separately, said Hermerén.

In preparing its opinion, the EGE rapidly concluded that there was no consensus on how best to define SynBio. However, Hermerén argued that we should not become bogged down in arguments over definitions: the lack of agreement was linked to the fact that definitions were needed for different purposes, as well as to the different avenues of SynBio research underway.

The notion of standard components in SynBio needs to have a caveat attached in that these can behave differently in different environments. This undermines the analogy between SynBio and engineering and could lead to safety risks, since for instance the same technology could be used to synthesise pathogens based on their DNA sequences.

Much of the EU regulatory framework already in place for biotechnology is relevant for SynBio. This includes regulations governing biosafety (Directive 2001/18/EC on the Deliberate Release into the Environment of Genetically Modified Organisms) and biosecurity (the EU's 2005 Counter-Terrorism Strategy addresses the risk of terrorists acquiring biological materials). Relevant regulations and guidelines have also been put in place by the World Health Organisation (WHO) and the World Trade Organisation (WTO).

In terms of an ethical framework for SynBio, the point of departure is the body of conventions and declarations on fundamental rights and human dignity adopted by the UN, UNESCO (the United Nations Educational, Scientific and Cultural Organisation), the Council of Europe and the EU (especially the Charter of Fundamental Rights, which became legally binding with the entry into force of the Lisbon Treaty in 2009. An ethical framework for SynBio must thus be established through a human-rights-based approach.

The choice of terminology is key to enabling a calm and rational discussion of these issues. In particular, we must distinguish between life as a scientific concept and 'Life' as an abstract, ambiguous and vague showstopper. Rather than easily reverting to phrases like 'patents on Life' or 'creating Life', we should be specific about the kinds of living organisms or forms of life we are talking about. 'Higher forms of life' in SynBio terms are bacteria, not humans or primates, and this should be made clear in communication aimed at a non-specialist public.

Similarly, terms like 'manipulating nature' can create an instinctive reaction that what is being talked about is unethical, yet few would question the ethics of eliminating smallpox or intervening to prevent suffering. The manipulation of the

mosquito genome has no moral equivalence to the manipulation of the human genome. We must make clear, therefore, why something is morally unacceptable and distinguish between biological stewarding for human purposes and exploitation.

The main ethical issues in SynBio are: safety; security; dual use (e.g. synthesising pathogens such as smallpox for medical research or for terrorism); environmental impact; justice; patents; and commerce. However, other issues also require consideration, such as the impact of SynBio research on the man-machine distinction, or ensuring that the conditions are in place for a transparent and constructive dialogue with the public. This dialogue needs to be sophisticated, engaging different stakeholders in a discussion about concerns, opportunities and development and the future direction of SynBio research.

Identifying concerns and ethical issues is not a neutral process, but depends on the evolution of scientific trends, on our own values, on what we want to achieve and what we wish to avoid. Also, distinct ethical issues must be addressed at different stages of work in SynBio, for instance: creating the first fully autonomous protocell in a lab; creating protocells that could survive outside the lab; releasing those protocells outside the lab; or creating protocells that are toxic or infectious. Similarly, many of the ethical issues that SynBio raises are relevant to specific sub-fields or to different points in the research timeframe (now, within five to ten years, or further ahead).

Governance issues

In terms of governance, Hermerén pointed out some issues raised by SynBio (safety, environmental impact, patenting or fair access to benefits) are not specific to it but are also pertinent to biotech or nanotech. These can, in principle, be addressed through regulation. Others, such as accountability, reductionism, or the impact of hype and hubris, require different approaches.

As such, there is no single answer to the question of how to govern SynBio, but several possible solutions, depending on the problem. At this stage, there are more questions than answers:

- Is existing regulation sufficient? Where are there overlaps and gaps?
- To what extent is monitoring, certification, registration and labelling required for SynBio products?
- How can a fruitful public dialogue be nurtured? What is the role of the media?
- To what extent should the EU be guided by the precautionary principle in its approach to SynBio?
- How can we encourage the beneficial use of SynBio and prevent misuse?
- How can we prevent misuse of SynBio research without introducing censorship of publications?

At the same time, Hermerén made the following assertions:

- The EU's policy on chemical, biological, radiological and nuclear security provides a valuable but insufficient basis for an approach to SynBio.

- We should consider establishing a centralised database of all DNA synthesisers.
- All institutes and research groups dealing with SynBio applications within the biosecurity and biodefence areas should need to be licensed.
- Existing conventions on the development, production and storage of biological weapons should be revised to incorporate provisions on SynBio.
- The artificial separation of safety, security and ethical issues should be avoided, since safety and security standards are not ethically neutral, particularly when they impose restrictions on the freedom of others; the same is true of the separation of ethics and intellectual property rights.
- While self-regulation of SynBio has the benefit of flexibility, independent monitoring and some regulation will also be needed. However, as a first step, the European Commission should take the initiative to have a code of conduct drawn up by SynBio stakeholders.
- Any approach to regulating SynBio should be global, rather than involving only the EU and US.

For his part, Dirk Stemerding, Senior Researcher at the Rathenau Institute in the Netherlands, presented three key lessons for the governance of SynBio:

- Governments must address regulatory concerns actively in order to sustain public trust in risk governance.
- The public debate on SynBio should be broadened to encompass the opportunities offered, with all stakeholders brought into the conversation.
- We must make sense of society's broader concerns about 'soft' impacts of SynBio, both in the context of particular applications and in the context of more general developments and trends.

The approach of the European Commission's DG Research

Peteris Zilgalvis set out the approach of DG Research to ethics and governance of emerging technologies and explained how this was being applied to SynBio.

Converging technologies such as SynBio are rapidly moving targets, hard to confine and define, said Zilgalvis. As such, designing an adequate regulatory framework for them, and doing so in a timely manner, is a major challenge.

The instruments available range from binding legislation to "soft law" measures (like codes of conduct, guidelines, best practice benchmarking) and engagement approaches (upstream engagement, stakeholder dialogue and societal deliberation). The experience with GMOs shows that regulating through binding legislation alone is insufficient, however. A complex new technology merits a complex mix of regulatory instruments.

The philosophy of DG Research, said Zilgalvis, is based on an upstream dialogue with stakeholders aimed at internalising ethical and social aspects in the design of new products and practices. In concrete terms, this means support for engagement and soft-law approaches which deal with a wider range of issues than risk assessment. Through the Seventh Framework Programme, the Commission is funding two specific research projects on the ethical, legal and social aspects of

SynBio – Synth-Ethics (which focuses in particular on biosafety, biosecurity and notions of life) and Sybhel (which aims to evaluate the impact of SynBio on human health and wellbeing).

Zilgalvis concluded by outlining some of the key challenges associated with a soft law/engagement approach to SynBio:

- *Timing:* move too early and there will be little societal and political interest; move too late and the debate will already be polarised
- *Framing:* bottom-up (with the risk of stakeholders hijacking the process and insufficient connection to the policymaking process) or top-down (with the danger of too much government control and insufficient connection to public concerns)?

Further research into public and stakeholder concerns in relation to SynBio is needed in order to be able to navigate these challenges and choose an optimal approach, Zilgalvis argued.

Lessons from nanotechnology for SynBio governance

Françoise Roure, Chair of the Technologies and Society Committee of the French High Council for Industry, Energy and Technologies, outlined some of the links and lessons to be learned for SynBio governance from the nanotechnology experience.

Both nano and SynBio, said Roure, are transformative, platform technologies, linked by high levels of complexity and uncertainty, and posing similar ethical and governance challenges.

Roure offered four key conclusions to her presentation:

1. Governance issues must be addressed through dialogue at all administrative levels, in order to lower the level of uncertainty and secure investments.
2. Inclusiveness and information sharing are critical, as opinions based on misperceptions can rapidly undermine trust and hamper innovation.
3. All stakeholders should invest in a 'governance continuum' involving joint assessments and methodologies to handle differences of view and manage conflicts.
4. Policymakers must have a high level of awareness of the issues at stake as their decisions impact industry, skilled jobs, safety and security.

In an EU suffering from high levels of unemployment as a result of the economic crisis, a new governance paradigm for emerging technologies such as nano and SynBio could pave the way for an attractive model of reindustrialisation and green growth, Roure emphasised.

Biosafety challenges

For Markus Schmidt of the Vienna-based Organisation for International Dialogue and Conflict Management, there are three main challenges stemming from SynBio in terms of biosafety:

- Are existing risk assessment methods valid for evaluating the new scenarios SynBio creates? If not, how should these methods be adapted?
- Can we use SynBio to improve the existing biosafety situation – and to carry out biosafety engineering in a better way?
- How do we deal with the risk of non-professionals gaining access to SynBio technology?

Schmidt said SynBio could be divided into five main sub-fields:

1. *DNA synthesis:* the ability to write DNA on a larger scale, faster and more cheaply than ever before
2. *Biological circuit construction or enhanced metabolic engineering:* reconstructing or rewiring metabolic pathways (sometimes using standard biological parts) to engineer whole genetic systems
3. *Defining the minimal genome:* taking an existing organism and reducing the genome to its bare minimum, enabling us to better understand the origins of life
4. *Developing protocells:* creating living (or lifelike) entities from the bottom up from inanimate chemical matter
5. *Chemical SynBio:* changing the basic biochemistry of life to come up with new and different software and hardware, creating a new biological enclave which cannot interact with the natural world.

The diversity of these five sub-fields means that a case-by-case approach must be taken to tackling questions of biosafety, Schmidt emphasised.

SynBio and society

Dorothée Benoit Browaeys gave the seminar an overview of the work undertaken in France by the NGO VivAgora to promote debate in society around SynBio. In 2009, VivAgora organised a series of debates – Engineering the Living 2.0 – which focused on the cognitive, societal, ethical, governance and economic issues raised by SynBio and on possible policy responses to these issues.

A key aim was to facilitate dialogue between stakeholders with different expertise and positions, while avoiding polarisation between technophiles and technophobes. Among the questions raised in the series of debates where the following:

- Does SynBio raise different concerns to GMOs and are GMO regulations applicable to SynBio?
- What are the motivations of SynBio pioneers, users and clients?
- Is SynBio science or engineering; how much of it is hype or bluff?
- What are the prospects of creating a durable living organism?
- How can SynBio revolutionise biology itself?
- Could free access to genetic sequences be a threat?

- Is a global system of governance for SynBio feasible? How should it look and who should be in charge?

Through encouraging the inclusion of citizens in techno-scientific decision-making bodies and supporting stakeholder dialogue, VivAgora's aim was to explore responsible innovation practices, Benoit Browaeys said.

For Michele Garfinkel of the policy research unit at the J. Craig Venter Institute, there are five key areas of societal concern related to SynBio – or more precisely, synthetic genomics, where the focus of the institute's work lies.

1. Bioterrorism. Could synthetic genomics lead to new ways to obtain pathogens or increase the resistance of pathogens to known treatments? Here, the issue is related to information being readily available and the inability take it back.

2. Biosafety. What if something gets out of a lab and replicates, contaminating a nearby community? There is a concern that researchers who are new to the field of biology – namely, engineers – are insufficiently sensitised to such dangers.

3. Harm to the environment. What if a bacteria escapes into the broader ecosystem? Do the speed, scale and power of this technology demand specific safeguards to prevent environmental contamination, above and beyond rules already in place?

4. Distribution of benefits. Should the technology be patentable or open source? Are there too few players on the market? These are concerns that are for the most part common to all emerging technologies.

5. Ethical and religious concerns. What is the effect of hubristic statements about playing God? What are the implications of changing the relationship between humans and nature? The construction of a free-living organism from chemicals adds a new element to an existing concern.

Garfinkel and three other researchers – Drew Endy, Gerald Epstein and Robert Friedman – have published an extensive report on 'Synthetic Genomics – Options for Governance'. The report addresses in detail the first two areas listed above (bioterrorism and biosafety) and puts forward a series of policy options. The J. Craig Venter Institute is currently undertaking a study into the other three areas.

Security implications

Piers Millett of the Implementation Support Unit for the Biological Weapons Convention in Geneva gave a series of insights into SynBio from the standpoint of biosecurity. His opening point was that he believes SynBio has too much potential to do good for it to be subjected to restrictions that would impede its development – something that would in any case probably not be practically possible. Rather, the only option available to us is to try to help shape the space in which SynBio matures.

A cursory glance at SynBio reveals that it has security implications:

- Through abstraction, the technical barriers to being able to use biology are lowered – including for those who would use it to do harm.

- Through characterisation, the unpredictability of biology-based technology is reduced, making it more reliable – and potentially improving the utility of biological weapons.

- Through standardisation, the distance between having an idea and developing a technology is reduced – narrowing the window to detect and interdict those who intend to use biology to cause harm.

However, not all SynBio's security implications are negative, nor will they manifest themselves in the same time frame or have the same impact.

Millett listed five facets of SynBio with have particular implications for security:

Types of malign use:

Three different types of user of SynBio for malign purposes could be envisaged: countries, groups or individuals. These in turn could use SynBio for three types of malign activity: warfare, terrorism, or crimes. States seem to be the most likely to emerge as malign users of SynBio, given their resources and the history of states applying new scientific expertise to develop new weapons systems. Terrorist groups, on the other hand, would seem to be unlikely to invest time and money in developing artificial agents when there are so many natural diseases available. There is also only a slight chance of an increase in the use of biological weapons by individual criminals – through the reinvigoration of the amateur and DIY biology communities which span off from the early SynBio movement.

Proliferation of resources:

With SynBio becoming more of an information science, the spread of data around the world has already accelerated to such an extent that 'the genie is already out of the bottle'. Biology is increasingly collaborative and international, and with barrier to entry being lowered through SynBio, it is being spread to new sectors of society within countries too.

The impact of the SynBio community itself:

The SynBio community remains a relatively small, defined group with which engagement can take place on an ah-hoc basis – but this will not remain the case for long and a more structured approach to outreach will soon be needed. The SynBio community is open to new ideas and approaches and to rational argument; it is committed to preserving its science and keen to avoid another GMO-type debacle occurring; and it is keen to avoid heavy-handed regulation – with some individuals likely to circumvent it should it be put in place.

SynBio as a tool to strengthen security:

More biology, being done in more places by more people also means more opportunities to develop new defences. Advances in understanding mechanisms of disease mean new prophylaxis and treatment options. Improvements in transitioning from science to technology reduces the time taken to respond to new threats. And further commercialisation of the science means more resources for detection, protection and decontamination technologies. Overall, there is great awareness of the security implications of SynBio within the community.

The possibility of developing a real biological engineering discipline:

It is in the longer term that the real security implications of SynBio lie. What if SynBio evolves so that we can write genetic code as easily as we can now read it; that we develop a comprehensive knowledge of all of the genome sequencing we have done; obtain a reliable way to control the functioning of biological systems;

and package it all together so that we can simply input what we want and produce a biological entity programmed to do it.

The security implications of reaching this stage of sophistication in SynBio would be manifold. The technology would have become too important and useful for anyone to try to get rid of it; it would be in such vast demand that it would be beyond the scope of a comprehensive control regime; and international efforts to police biology through verification would become impossible due to the size of the problem. Furthermore, traditional difficulties in differentiating between permitted and prohibited activities would be further blurred.

In the long run therefore, SynBio will force the security community to rethink how biology is policed. There will be a paradigm shift away from trying to regulate this technology to trying to manage it. The most likely outcome may be something along the lines of how the internet is policed in democracies: a laissez faire approach combined with strict rules to prevent a small number of illicit activities. We should therefore focus less on control regimes and more on outreach.

A screening framework for use by double-stranded DNA providers

Jessica Tucker, a contractor serving as a Senior Policy Analyst supporting the United States Department of Health and Human Services, gave an overview of the screening framework guidance developed for use by synthetic double-stranded DNA providers. The US government recommends that all orders for synthetic double-stranded DNA (that is 200 base pairs in length or greater) be subject to a screening framework that incorporates both sequence screening and customer screening.

The initiative was the result of a 2006 report by the National Science Advisory Board for Biosecurity, which recommended that the US government implement a screening process for providers of synthetic DNA. The context was the synthesis of the polio virus (in 2002) and of 1918 influenza, as well as other incidents which raised concerns about the biosecurity implications of SynBio and biotechnology more broadly.

The development of any oversight mechanism, Tucker said, must balance the need to minimise the risk of misuse with the need to encourage science and innovation. It was also essential to involve relevant industrial players, the scientific community and other stakeholders, she stressed.

Risk assessment and risk governance

According to Göran Hermerén, an assessment of the potential harms and benefits of SynBio must take into account the relative certainty and uncertainty of each of these. Safety is not a black and white issue and the degrees of acceptable risk have to be related to other variables. Key questions to be asked included:

- What do you want to achieve and what do you wish to avoid?
- Are the risks ethically acceptable?
- Is the distribution of risks and benefits arising from various applications equitable – in particular in terms of applications requiring interaction between natural and synthetic organisms?

- What are the implications of such interaction for human health, animal health and welfare, and the environment?

Risk Assessment

For Jim Bridges, Chair of the EU Scientific Committee on Emerging and Newly Identified Health Risks, there are a number of parallels between the challenges in assessing the risks posed by SynBio and those posed by nanotech: a rapidly changing database, a great range of potential applications and very limited information on health and environmental aspects. According to Prof. Bridges, risk assessment for SynBio entails the following four steps:

1. Characterisation of the relevant physical and chemical properties of each product or process, along with its biological properties
2. Assessment of the potential exposure of humans, animals and the environment under expected and misuse conditions
3. Examination of the hazardous properties
4. Estimation of the risk

Risks posed to humans through exposure to SynBio products must be assessed in different situations: to researchers during the R&D phase; to workers during manufacture; to consumers and/or others during use; to workers and others during inactivation, disposal or re-use.

The assessment must also be based on four scenarios: zero exposure (effective containment); some exposure but little likelihood of absorption; absorption will occur but is likely to be limited and clearance should be rapid; absorption will occur and the SynBio product or a 'metabolite' may persist in the body. Equally, environmental exposure could entail no release of the SynBio product; very localised release; widespread release but rapid degradation; or widespread release and persistence.

Building on the chassis analogy with car manufacturing, mentioned in Prof. Kitney's keynote presentation, Prof. Bridges noted that - as it is imperative nowadays to consider safety as an integral part of car design - the same approach should be used for engineered biological material. Indeed, engineered biological material should be designed with safety in mind.

An integrated approach

There is no reason to assume that SynBio products will have common hazardous properties, Bridges pointed out. As such, for the foreseeable future, they will have to be considered on a case-by-case basis, as is the case with nanotechnologies. Common working definitions, data-reporting protocols and codes of practice must be developed, along with effective, sustainable procedures for the early provision of relevant information to risk assessors and frequent stakeholder discussions. A common framework for considering risks and benefits of SynBio products must be developed.

Above all, Bridges argued, work on safety, health and environmental aspects is properly funded and integrated into SynBio research from the beginning. They must be an integral part of design, development and industrialisation and take into account the full life cycle, including scenarios of misuse.

Risk governance deficits

Joyce Tait of the University of Edinburgh outlined the work of the International Risk Governance Council (IRGC) on risk governance in SynBio. An appropriate approach to risk, she argued, would be one that enables innovation, minimises risk to people and the environment, and balances the interests and values of relevant stakeholders.

The IRGC approach to risk governance promotes regulatory certainty as a means to stimulate commercial investment, along with smarter regulation to enable innovation without compromising safety. It also seeks to reconcile stakeholder needs and concerns, such as ignorance and uncertainty about future benefits and risks, as well as volatile public opinion over a long time scale.

Regarding SynBio specifically, Tait outlined the risk governance deficits (deficiencies or failures in risk governance, as well as weak spots in risk assessment and management) in four areas:

Technology development:

- Investments are being made with public benefits in mind but with insufficient consideration of how these will be delivered.
- Early developments are likely to be an extension of GM technology, particularly when it comes to biofuels.
- Pharmaceutical companies are reluctant to invest in SynBio at present, as the benefits are not yet obvious.
- There is no clear value chain as yet for most SynBio developments.

Policy and regulation (early process stage):

- Regulatory efforts should not be wasted on developments which will not stand the test of time.
- We should remain alert to potential risk government deficits from future developments.
- There is a need for a robust and flexible regulatory approach, given the range of future uncertainties.
- International dialogue on the appropriate scale and timing of regulatory oversight is required.

Policy and regulation (product development stage):

- It is difficult to handle the joint goals – delivering public benefits, avoiding unacceptable risks and enabling commercially viable activity in a future-oriented context.
- Collaboration is needed to develop regulatory systems for foreseeable risks.
- Effective responses must be prepared for unforeseen risks or rogue behaviour.
- Heterogeneity is required in a field with many different techniques and applications.

Public and stakeholder engagement:

- We must develop a strategy on how and when to incorporate stakeholder inputs into governance decision-making.
- Risk governance deficits inherent in the process of 'upstream engagement' should be considered.
- We should reflect on whether engagement is capable of resolving the societal issues raised by SynBio.
- An equitable approach should be taken to pressure groups arguing for and against particular developments

Tait emphasised the potential of regulation to shape an industry sector that is developing a new technology, citing the examples of GM crops and stem cells. An onerous and time-consuming regulatory system, such as that in place for chemicals or pharmaceuticals, will inhibit innovation and discourage small companies from developing products other than those demanded by multinationals. Novel and pathbreaking technologies will be far less likely to emerge.

Public opinion

Eléonore Pauwels, a public policy scholar working on the Synthetic Biology Project at the Woodrow Wilson International Center for Scholars, gave an overview of public perceptions of SynBio.

Popular unease about science remains widespread, with the controversy over the perceived undesirability of GM crops still unresolved after more than a decade. With some of the groups that led the charge against GMOs already mobilising to fight SynBio, public engagement cannot be left to chance – and the press cannot be counted on to present in an accurate manner the science and its implications, said Pauwels. Stakeholders must ask themselves which SynBio applications might prove acceptable to the public, and what risks will prove acceptable to society at large. Key decisions will have to be made over the next two or three years on how to engage with the public, how to address the concerns of increasing numbers of NGOs, and how to provide social oversight, both nationally and globally.

According to research carried out in the US on behalf of the Wilson Center, public awareness of SynBio more than doubled between 2008 and 2009, with the proportion of Americans saying they heard either a lot or something about SynBio increasing from 9 percent to 22 percent, while those saying they had heard nothing at all fell from 67 percent to 48 percent. Yet this is not necessarily good news for proponents of SynBio, as research has also shown a 16 point increase in Americans believing that the risks outweigh the benefits of the science once they are provided with information about it. Americans' top concerns about SynBio are related to biosecurity and moral concerns about creating artificial life.

The key factors in driving public perceptions are framing and analogies – to cloning, stem-cell research and genetic engineering. People trying to understand emerging technologies will fall back on narratives they feel comfortable with long before they pick up a biology book or try to understand the science. The SynBio story fits with cultural narratives that have been developed for previous technologies such as nanotech – such as 'opening Pandora's Box' (corrupting or manipulating science for evil purposes), 'messing with nature' or 'playing God'.

What are the principle communication challenges for SynBio? While presentation of the technology is vital, it can also be a liability. There is considerable potential for risk amplification, linked to the following factors:

- the difficulty of communicating on biological issues, biosafety and biosecurity
- the high potential for ill-informed coverage in the press
- the fact that enduring narratives are about failures of regulators to anticipate or provide adequate oversight, be it in relation to food, drugs or finance

Pauwels highlighted two key lessons arising from the Wilson Center's research. The first is that applications matter. More than half of US adults supported research on synthetic organisms aimed at producing more efficient biofuels, even after receiving information on the potential risks. The second is that we need to open up the politics of governing innovation and to bridge the trust gap with the public by showing that regulators are aware of SynBio and its implications. In the short term, Pauwels called for more applied international research on public perceptions of SynBio, based on which a public engagement strategy should be implemented.

Patenting

Under what conditions and circumstances can SynBio applications be patented?

The November 2009 EGE Opinion on the Ethics of Synthetic Biology contained two recommendations in relation to the patenting of SynBio applications:

- There should be a debate on what can be the object of a patent and what should be available through open access, with a view to finding the most appropriate way to ensure public access to the results of SynBio.
- The European Patent Office (EPO) should refer contentious ethical issues of general relevance to the EGE for consideration, particularly if a class of inventions that ought not to be directly exploited commercially needs to be defined.

According to Berthold Rutz, biotech expert at the European Patent Office (EPO) in Munich, SynBio probably does not herald anything new from a patenting point of view. The patentability of biotechnological inventions in Europe is governed by the provisions of the European Patent Convention (EPC), an intergovernmental treaty signed by 37 states, and by the EU directive on the patentability of biotechnological inventions (98/44/EC).

In line with these provisions, patents have been granted for many years for nucleic acids, proteins, vectors, cells and micro-organisms, as well as claims for compound-synthesising methods, uses of micro-organisms for synthesis, and synthesising apparatuses.

Most SynBio applications will constitute biotechnological inventions according to rule 26 of the European Patent Convention (EPC), which defines these as products 'consisting of or containing biological material or a process by means of which biological material is produced, processed or used', while biological material is

defined as 'any material containing genetic information and capable of reproducing itself or being reproduced in a biological system'.

Rule 27 of the EPC defines patentable biotechnological inventions as:

- Biological material which is isolated from its natural environment or technically produced even if present in nature (nucleic acid molecules, proteins, cells etc)
- Plants or animals if not confined to a particular variety, e.g. transgenic plants or animals
- Microbiological processes and products, e.g. micro-organisms

A particular issue is the patentability of BioBricks, or standard biological parts, which are a key element of SynBio. Should these be patentable or could this potentially hinder innovation as alleged by some? As Dr Rutz argued, this debate is conditioned by the fact that many of these biological building blocks have already been patented. Moreover, patented parts can be licensed or made accessible through patent pools.

Roundtable debate

During the concluding session of the workshop, Vitor Martins dos Santos summarised the key elements emerging from the discussion on the opportunities and challenges associated with SynBio:

- SynBio combines major disciplines but is also about transforming biotechnology into a true engineering discipline.
- Its impact on diverse sectors could be comparable to that of ICTs.
- Analogies can be misleading and should not be taken literally; unlike Lego bricks, biological components are dependent on their context and subject to Darwinian evolution.
- The development of international standards and registries will be key to empowering the engineering of useful system composed of parts, chassis and composable models. However, standards are a means, not an end in themselves.
- SynBio faces four types of challenge: scientific, technological, organisational and societal.
- There are no synthetic micro-organisms in sight for now – only DNA molecules.

As regards ethics and governance, Göran Hermerén suggested that the following seven points encapsulated the discussions that had taken place in the workshop:

- For most practical issues, we can be pragmatic when it comes to definitions of SynBio; however, for regulatory purposes we will need to agree more precise wording.
- Analogies between GMOs, nanotech and SynBio can be useful in terms of certain key lessons, but we should not downplay the differences either.
- Research on the social, human and ethical aspects of SynBio must be integrated into the scientific discipline from early on.
- Different approaches to SynBio will raise different problems.
- A strategy for public engagement on SynBio will be important and should be guided by lessons from past mistakes in terms of bridging the trust gap and understanding the role of the media.
- The SynBio discussion must be a global one, reflecting the global nature of the science and the marketplace for applications.
- A better framework for risk/benefit assessment is needed, given the level of uncertainty surrounding both.

Among the other recurring themes in the workshop which were again highlighted during the concluding discussion were the following:

- The idea that SynBio represents a paradigm shift in science and has the potential to lead to a new relationship between man and nature

- The need to involve all stakeholders in the process of deciding on a governance framework for SynBio
- The need for any EU-sponsored or facilitated code of conduct to be drawn up by scientists themselves rather than policymakers
- The importance of improving our understanding of public perceptions of SynBio through serious investment in research focusing on different publics in different national contexts
- The desirability of ensuring that the SynBio conversation is discussed in terms of benefits as well as risks

Conclusions

What conclusions can be drawn from these two intensive days of discussion on SynBio? Many speakers considered it important to agree a definition of this area of science, while others were more relaxed on this point, arguing that definitions could vary depending on their purpose. For instance, is a definition needed in order to attract public funding or venture capital, for labelling or for risk assessment purposes? While the workshop may have arrived at a non-conclusion on this point, it did become clear that SynBio's uniqueness is derived from the combination of a number of elements and disciplines; that it was not yet certain where the boundaries of SynBio lay; and that SynBio's multiple different orientations were overlapping and interdependent.

Ms Paola Testori-Coggi, Director General of the Health and Consumers Directorate (DG SANCO), tried to summarise at her closing remarks the major conclusions of this two-day workshop:

1. There is no single clear definition on Synthetic Biology and what is included under this term. In order to monitor the relevant developments, assessing possible benefits and risks and analyse the applicability of current regulations, there is a need to establish a clear definition for synthetic biology and its products. The European Commission should consider inviting the European standardisation bodies to start work in this area.
2. EU legislation exists in most if not all the areas related to the potential applications of synthetic biology. Nevertheless, due to the novel characteristics of synthetic biology, it is not clear whether the definition of the scope for such legislation would ensure legal certainty for the practical application to SB of all relevant legal instruments. Moreover, the requirements, tests and criteria of the existing legislation may not be adequate for SB. Therefore, a review of the regulatory framework should be undertaken at an early stage so as to adequately cover the current evolutions in this sector.
3. Synthetic biology comes with innovative promises of substantial benefits for health, the environment, resource management and the economy. Nevertheless, it is characterised by large uncertainties, potential risks and it raises ethical questions. In order to promote and sustain this innovative potential, there is a need for an appropriate risk - benefits analysis for facilitating a comprehensive assessment of this new technology.
4. Learning from previous experiences, it is particularly important that the EU research projects on synthetic biology include a systematic consideration of the relevant safety and ethical aspects.
5. SB is likely to raise public concerns similar to those of GMOs. There is clearly a need for early public engagement. To that aim, it is necessary to identify the appropriate "publics", as Ms Testori said, for such engagement.
6. The effective governance of synthetic biology requires a sustained dialogue as well as mutual understanding and mutual learning between all the relevant actors in the areas of science, risk assessment, ethics, decision making, industry, civil society.
7. A possible code of conduct for research along the lines of the EU code for research on nanotechnologies could be considered.

Finally, as Ms Testori said, the successful experience of the SB workshop should be repeated on a regular basis.

Appendix

List of main questions raised (and given elements of answer) at the Synthetic Biology: From Science to Governance Workshop, Brussels, 18-19 March 2010.

Definition

1. What is included under the term "Synthetic Biology"?
2. Is SynBio science or engineering; how much of it is hype or bluff?
3. How much Synthetic Biology different from existing disciplines and techniques (genetic engineering, nanotechnology)?

Research community

1. What is needed to strengthen the European SynBio researcher community?
2. How can we prevent misuse of SynBio research without introducing censorship of publications?

Governance

1. Is existing regulation sufficient? Where are there overlaps and gaps?
2. To what extent is monitoring, certification, registration and labelling required for SynBio products?
3. How can we encourage the beneficial use of SynBio and prevent misuse?
4. Is a global system of governance for SynBio feasible? How should it look and who should be in charge?
5. Should the technology be patentable or open source? Are there too few players on the market?
6. Under what conditions and circumstances can SynBio applications be patented?
7. Should these be patentable or could this potentially hinder innovation as alleged by some?

Communication

1. How can a fruitful public dialogue be nurtured? What is the role of the media?
2. To what extent should the EU be guided by the precautionary principle in its approach to SynBio?
3. What are the principle communication challenges for SynBio?

Ethics

1. What is the effect of hubristic statements about playing God?
2. What do you want to achieve and what do you wish to avoid?
3. Are the risks ethically acceptable?
4. What are the motivations of SynBio pioneers, users and clients?

Safety

1. Can we use SynBio to improve the existing biosafety situation – and to carry out biosafety engineering in a better way?
2. Does SynBio raise different concerns to GMOs and are GMO regulations applicable to SynBio?
3. What are the implications of such interaction for human health, animal health and welfare, and the environment?
4. Assuming that one would want to make SynBio "inherently safe," how could this be achieved and which aspects of a given SynBio application design, development, and production phase would this concern?

Risk Assessment

1. What if a bacteria escapes into the broader ecosystem? Do the speed, scale and power of this technology demand specific safeguards to prevent environmental contamination, above and beyond rules already in place?
5. Is the distribution of risks and benefits arising from various applications equitable – in particular in terms of applications requiring interaction between natural and synthetic organisms?
6. Are existing risk assessment methods valid for evaluating the new scenarios SynBio creates? If not, how should these methods be adapted?
7. How do we deal with the risk of non-professionals gaining access to SynBio technology?

Security

2. Could free access to genetic sequences be a threat?
3. Could synthetic genomics lead to new ways to obtain pathogens or increase the resistance of pathogens to known treatments?
4. What if something gets out of a lab and replicates, contaminating a nearby community?

Future perspectives

1. What are the prospects of creating a durable synthetic living organism? From existing biological past? From scratch?
2. How can SynBio revolutionise biology itself?
3. What are the up-coming major applications in the market?