Institute for European Studies
Vrije Universiteit Brussel

Policy | brief

Regulatory Gaps in the Global Governance of Synthetic Biology

Issue 2014/11 · December 2014

by Florian Rabitz

Synthetic biology is an emerging technology with potentially far-reaching benefits and risks. As a cross-cutting issue, different aspects of synthetic biology fall within the scope of different international agreements. Contemporary biosafety and biosecurity frameworks are characterized by important regulatory gaps which policy makers need to address to minimize risks that may arise in the future both from commercial use and weaponization. In some cases, this may require formal treaty amendments, whereas others can possibly be resolved at lower levels, for instance through interpretive statements of treaties' decision-making bodies.

Introduction

The field of genetics has seen many advances in the last 60 years: the discovery of the DNA double helix in 1953, recombinant DNA in the early 1970s; the development of the polymerase chain reaction in 1983; and the Human Genome Project between 1990 and 2003. Industrial applications are found in a vast range of fields, from genetic testing, biopharmaceuticals, vaccines and stem cell therapy, through biofuels and other industrial fermentation processes to biotechnologically-enhanced crops. While bringing significant benefits to society, modern biotechnology is also highly controversial, and poses a number of regulatory challenges. Recent developments in the field increasingly permit the deliberate design of genes, DNA strands, and even entire genomes. Such "synthetic biology" is currently an emerging technology. However, contemporary governance arrangements are partially inadequate to cope with the challenges the technology may pose once it finds widespread commercial application. Below, after giving a brief introduction to the technology itself, I identify such gaps in the international biosafety and biosecurity regimes. While regulation needs to be as unobtrusive as possible as not to hamper innovation in the field, precautionary decision-making in the area is required in order to address various risks, ranging from unregulated transboundary movements of biological materials to security risks associated with potential weaponization.

From recombinant DNA to directed evolution

The invention of recombinant DNA technology in the early 1970s allowed for the combination of genetic materials from different sources. Through the insertion of selected genes, host organisms could now be modified to display traits that were hitherto impossible to obtain via traditional breeding methods. For example, the insertion of genes responsible for the synthesis of beta-carotene into ordinary rice permitted the production of an improved variety ("Golden Rice") intended for agricultural production in regions with chronic vitamin A deficits. In medicine, recombinant DNA technology allowed the creation of a Hepatitis B vaccine by inserting a viral gene into yeast. For designing insect-resistant crops, genetic parts of the Bacillus thuringiensis bacterium have been used for endowing potatoes, maize or cotton with insecticidal properties. While all those applications involved the combination of existing DNA, recent technological advances allow for its de novo synthesis in the laboratory. Whereas traditional genetic engineering is "a cut and paste affair, in which biotechnologists shuffled pieces of DNA [...] between already existing species", contemporary synthetic biology has been likened to "the biological equivalent of word processors" (ETC Group 2011: 3). With computers, custom DNA sequences can now be built from inorganic chemical parts based on digital blueprints. The technology also allows for the removal of superfluous functions from a genome, and its subsequent customization to perform specific functions. While defining synthetic biology is difficult due to the variety of applications and scientific disciplines involved, a common distinction is

between more recent bottom-up approaches, which "create novel biochemical systems and organisms from scratch, using nothing but chemical reagents", and older top-down approaches, treating "existing organisms, genes, enzymes, and other biological materials as parts or tools" (Presidential Commission 2010: 36). While synthetic biology is still in its infancy, a number of commercially-viable applications nevertheless already exist. Those include the production of biofuels, molecules, essential oils, pharmaceutical products such as the anti-Malaria medicine Artemisinin, the influenza vaccine Tamiflu, or the antibiotic Cephalexin. At the same time, commercial providers are offering mail-order shipment of customized, synthetical DNA, and low-end oligonucleotide synthesizers for home use are available for less than 10,000 US$. The technology has numerous implications for international biosafety and biosecurity regimes, ranging from gaps in current treaties regarding synthetically-produced organisms and micro-organisms, to the security implications of do-it-yourself production of biological agents.

Implications for the international biosafety regime

Biosafety entails the regulation of biological materials intended for both contained use and deliberate release into the environment in the absence of an intent to harm. Usage of biological materials in laboratory settings is presently subject to a wide range of regulations, with the World Health Organization, the US and the European Union prescribing different biosafety levels depending on the potential hazards for workers and the risk of unintentional release of materials. It is presently unclear whether existing biocontainment standards will be sufficient for organisms produced via synthetic biology. However, laboratory safety does not require international action, as it can be sufficiently addressed at the domestic level. Presently, only a small number of facilities designated as the highest biosafety level (BSL-4) exist worldwide. Most of those are concentrated in industrialized countries such as Australia, Canada, Germany, Italy, Japan, the UK and the US, where domestic regulatory standards are already high. However, a risk is the "diffusion of technology, knowledge and capabilities beyond the professional biotechnology community" (Schmidt 2008), that is, to individuals without professional training and outside the tightly-regulated laboratory context. While such uses may require novel forms of regulatory oversight at the domestic level, they do not necessarily require new forms of international action.

Secondly, policy-makers increasingly recognize the risks of modern biotechnology intentionally released into the environment. Agricultural biotechnology, in particular, poses risks such as genetically modified organisms either outcompeting non-modified species or causing undesired mutations through gene transfer. Additionally, there is currently little insight into the toxicity and allergenicity of genetically modified food. In the European Union, concerns about the risks of modern biotechnology have led to strict regulations. Commercial releases of Genetically Modified Organisms (GMOs) are subject to prior risk assessment and require authorization by competent national authorities under the participation of Member States and the European Commission. All products consisting of or containing GMOs are traced throughout the supply chain, and any products placed on the market containing more than "adventitious or technically unavoidable" amounts of GMOs are subject to mandatory labelling (Regulation EC 1830/2003), and both the contained use and deliberate release of GMOs are subject to strict regulatory requirements (Directives 2009/41/EC and 2001/18/EC).

However, a number of important gaps exist in the international regulatory framework. Internationally, the primary treaties for biosafety are the World Trade Organization's (WTO) 1995 Agreement on the Application of Sanitary and Phytosanitary Measures and the 2000 Convention on Biological Diversity's Cartagena Biosafety Protocol. The former delimits the scope of WTO member states for restricting international trade based on considerations of food safety and animal and plant health. The latter agreement allows for precautionary decision-making in the import of "Living Modified Organisms" (LMOs), enabling member states to subject certain imports of those materials to an Advance Informed Agreement procedure. The Protocol does not currently have wide coverage, as a number of LMO exporting countries have not ratified it. It also possesses a number of gaps regarding synthetic biology: First, the Protocol's Article 3 definition of LMOs does not cover their constituent parts (i.e. plasmids and purified DNA). This allows for the cross-border transfer and subsequent assembly of LMOs outside of the Protocol's scope. Second, the Protocol does not include digital transfers of DNA sequences within its definition of "transit" and "transboundary movement". Where DNA can be synthesized domestically, based on sequence data received from abroad, this undercuts the Protocol's goal of ensuring that the "development, handling, transport, use, transfer and release of any living modified organisms are undertaken in a manner that prevents or reduces the risks to biological diversity, taking also into account risks to human health" (Cartagena Protocol Article 2.2). However, effective monitoring of such digital transfers is virtually impossible. Third and finally, the Protocol's Advance Informed Agreement procedure, allowing for import restrictions for LMOs based on precautionary decision-making and risk assessment, does not apply to LMOs intended for contained use. This raises the question of whether domestic biocontainment standards for organisms produced via synthetic biology are sufficient, or whether Advance Informed Agreement would be necessary for importing parties to judge the soundness of containment.

Gaps thus exist regarding the definition of LMOs under the

Cartagena Protocol, the regulation of domestic LMO synthesis based on sequence data received from abroad and, possibly, the import of high risk synthetic materials for laboratory use. Some of those issues are more easily resolvable than others. Regulating the transfer of sequence data is the most challenging, also with respect to biosecurity (see below). Regulatory gaps in the definition of LMOs might be addressed through an interpretative decision by the Meeting of the Parties to the Cartagena Protocol. For instance, whether plasmids, small DNA molecules existing independently from chromosomal DNA, count as "living" organisms or not is a matter of debate among biologists. Finally, whether an Advance Informed Agreement procedure is necessary for synthetic materials intended for contained use depends on their risks relative to non-synthetic LMOs.

Implications for the international biosecurity regime

Biosecurity refers to "the protection, control of, and accountability for high-consequence biological agents and toxins, and critical relevant biological materials and information, to prevent unauthorized possession, loss, theft, misuse, diversion, or intentional release" (NSABB 2010: 10). While international biosecurity regulations focus on the acquisition of biological weapons by states, recent technological developments increasingly allow for the manufacturing of such weapons by private actors. Concerns about biosecurity has intensified in recent years, with methods for genetically-engineering H5N1 influenza viruses directly transmissible between humans published in Science and Nature (Garrett 2013). A few years earlier, scientists were able to artificially reconstruct the genome of the H1N1 influenza strain responsible for the "Spanish Flu" which, at that time, caused at least 50 million deaths within a timespan of a few months. The increasing availability of sequence data is accompanied by the emergence of a broad range of commercial providers for synthesized DNA. In 2006, journalists working for the Guardian were able to obtain parts of the genome of the smallpox virus simply by placing a mail order with a commercial provider. In itself, knowledge of a DNA sequence plus access to synthesized genes is not sufficient for producing a viable pathogen. Resulting DNA needs to be transplanted into host cells, which require sufficient replication in order to yield effective amounts and, depending on the agent in question, the development of a delivery system may also be beyond the reach of nonstate actors. At the same time, the increasing technical ease with which pathogens may be synthesized, or enhanced for higher infectivity, better transmission or resistance to antibiotics or vaccines, poses significant challenges to the existing biosecurity regime.

Internationally, the main framework for biosecurity is the 1972 Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons (BWC). The Convention prohibits the development, stockpiling, acquisition and retainment by contracting parties of "[m]icrobial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes" (BWC Article 1, my italics). While the Convention's effectiveness is limited by the absence of a verification regime and imprecise obligations for domestic implementation, synthetically-produced biological weapons clearly fall under its scope. The international biosecurity regime has, in recent years, shifted from focusing on disarmament to preventing and responding to utilization by non-state actors (Kelle 2007). The chemical weapons attack on the Tokyo subway in 1995 and the 2001 Anthrax attacks in the US fueled a discourse centered on the usage of weapons of mass destruction by nonstate actors, rather than states. Biological warfare became to be perceived as a threat to the general population, instead of merely the armed forces. This led to strong linkages developing between the biosecurity and public health regimes. The World Health Organization's (WHO) recently revised International Health Regulations (IHRs) to oblige each state party to notify the organization in case of an "unexpected or unusual public health event within its territory, irrespective of origin or source, which may constitute a public health emergency of international concern" (IHRs Article 7, my italics). The WHO's 2011 Pandemic Influenza Preparedness Framework builds on the notification requirements under the IHRs, obliging member states to share influenza virus strains with WHO-designated laboratories for the rapid development of vaccines. Finally, the WHO has recently been holding informal consultations on Dual Use Research of Concern in the issue area. Increasing fears of bioterrorism are thus accompanied by the development of strong linkages between the biosecurity and public health regimes.

Historically, very few instances exist of states using biological weapons. While future uses by states cannot be ruled out, the present challenge for international biosecurity arises from the ease with which nonstate actors may be able to manufacture "home-brewed" bacteriological or viral agents. Regulatory gaps exist less in the response to such attacks, but rather in their prevention. International harmonization of domestic regulations may be required for addressing transboundary movement of synthesized DNA offered by commercial providers. The gaps in the Cartagena Protocol regarding constituent parts of LMOs, discussed above, are equally relevant for transboundary movement of materials intended for weaponization. This would prevent the acquisition of materials from jurisdictions with relatively low regulatory standards. A second challenge arises not from physical transport, but from the electronic transfer of DNA sequence data allowing for the domestic production of biological agents. Regulating the transboundary exchange of digitalized genetic codes may turn out to be impossible, considering that such information is increasingly becoming part of the public

domain. Proposals have been made for commercial providers of synthetic DNA to use standardized computer software for determining whether customers are ordering material suitable for weaponization. Within the United States, a voluntary scheme exists for the screening of customers, which could be a basis for international harmonization in order to, again, prevent potentially dangerous materials from being acquired in jurisdictions with insufficient domestic regulation.

Conclusions

Synthetic biology is an emerging technology that has not yet been widely marketized. Nevertheless, present institutional arrangements on the international level are in some respects insufficient to deal with the potential future risks the technology might pose. In particular, gaps exist regarding the transboundary movement of purified DNA, electronic transfers of sequence data, as well as the surveillance of commercial providers offering custom-tailored DNA. While the securitization of global health politics raises a number of problems in itself, an increased focus of health governance on risks associated with biological agents may provide appropriate response measures for both intentional and unintentional releases of new biological hazards.

As with other emerging technological developments, from nanotechnology, 3D printing and fully-autonomous robots to geoengineering, synthetic biology holds both risks and promises. Similar to chemistry and nuclear technology, one major challenge is the dual-use problematique, particularly if synthetic biology will allow determined nonstate actors to manufacture weapons of mass destruction at limited costs. Yet the commercial application of high-risk technology also entails significant regulatory challenges.

Policy-makers have increasingly acknowledged in recent years that risks are frequently unknown, and that regulation may be required even if neither probability nor costs of catastrophic events may be quantifiable. Accordingly, precautionary decision-making is required to balance risks and benefits. For example, several provisions of the Cartagena Protocol could be clarified through decisions by its Meeting of the Parties. Furthermore, soft law instruments or private regulations, such as non-binding international codes of conduct for commercial providers of synthetic DNA could be developed. However, depending on the pace and scope of technological development, more far-reaching and institutionalized forms of international regulation (e.g. formal amendments to existing international agreements or even the negotiation of new ones) may be required in the future.

References

ETC Group. (2011) The New Biomassters: Synthetic Biology and the Next Assault on Biodiversity and Livelihoods. Action Group on Erosion, Technology and Concentration Communique # 104.

Garrett, L. (2013) Biology's Brave New World: The Promise and Perils of the Synbio Revolution. In: Foreign Affairs 92(6): 28-46.

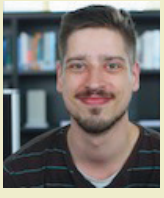
Kelle, Alexander. "Securitization of international public health: implications for global health governance and the biological weapons prohibition regime." Global Governance: A Review of Multilateralism and International Organizations 13.2 (2007): 217-235.

NSABB. (2010) Addressing Biosecurity Concerns Related to Synthetic Biology. Report of the National Science Advisory Board for Biosecurity.

Presidential Commission for the Study of Bioethical Issues. (2010) New Directions: The Ethics of Synthetic Biology and Emerging Technologies. Washington D.C.

Schmidt, Markus. "Diffusion of synthetic biology: a challenge to biosafety." Systems and synthetic biology 2.1-2 (2008): 1-6.

About the author



Florian Rabitz was a doctoral researcher at the IES from 2009 until 2014 within the FWO project "governing through regulatory complexes: the European and international management of genetic resources". He is currently a visiting Professor at the Institute for International Relations, University of São Paulo, working primarily on international environmental regimes and intellectual property rights.

Policy briefs are published by the
Institute for European Studies
Jean Monnet Centre of Excellence
at the Vrije Universiteit Brussel

www.ies.be
Pleinlaan 5
B-1050 Brussels
T +32 2 614 80 01
ies@vub.ac.be