Chapter 3
Opportunities, Challenges, and Future Considerations for Top-Down Governance for Biosecurity and Synthetic Biology

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3.1 Introduction

Synthetic biology promises to make biology easier to engineer (Endy 2005), enabling more people in less formal research settings to participate in modern biology. Leveraging advances in DNA sequencing and synthesis technologies, genetic assembly methods based on standard biological parts (e.g. BioBricks), and increasingly precise gene-editing tools (e.g. CRISPR), synthetic biology is helping increase the reliability of and accessibility to genetic engineering. Although potentially enabling tremendous opportunities for the advancement of the global bioeconomy, opening new avenues for the creation of health, wealth and environmental sustainability, the possibility of a more 'democratic' (widely accessible) bioengineering capability could equally yield new opportunities for accidental, unintended or deliberate misuse. Consequently, synthetic biology represents a quintessential 'dual-use'

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biotechnology – a technology with the capacity to enable significant benefits and risks (NRC 2004).

In relation to existing top-down governance[1] measures for biosecurity,[2] synthetic biology represents a promising yet potentially destabilizing advancement in the life sciences, one that could introduce new risks and regulatory challenges. In particular, a number of high-profile synthetic biology experiments, ranging from the *de novo* synthesis of poliovirus (Cello et al. 2002) to the recent synthesis of horsepox virus (Noyce et al. 2018), have raised concerns that the same techniques could be exploited to bypass regulatory controls (e.g. the United States, US, Select Agent Regulations) on lists of high-risk pathogens. Moreover, the possibility of synthesizing novel 'taxonomically unclassified' pathogens (NSABB 2006; Garfinkel et al. 2007) has led some to question the logic and utility of current 'list-based' approaches to regulation. Looking to the future, if synthetic biology does, in fact, 'deskill' the 'art' of biological engineering, new regulatory approaches could very well be essential because the tools of modern biology will be widely accessible to both responsible and malicious actors.

Claims about synthetic biology's potential, like other emerging technologies, nonetheless tend to overstate its 'enabling' capacity. Likewise, the ease of producing biological weapons tends to be overstated. As a number of commentators note, biology is not yet easy to engineer (Jefferson et al. 2014) and, for the foreseeable future, the skills necessary to produce biological weapons are likely to remain only within the grasp of states (Piers Millet in Regalado 2016). However, the field's emphasis on eliminating technical barriers and reducing the importance of tacit knowledge (Oye 2012) represents a powerful source of expectation for advocates and critics alike. For advocates, it represents the possible realization of modern biology's full potential, one that could yield revolutionary advances in health, medicine, and industry in the twenty-first century. For critics, it represents a seemingly open-ended risk that requires exceptional precaution. For national governments, and international conventions responsible for establishing global biosecurity norms and obligations that are operationalized at the national level through legislation and other regulatory tools (McLeish and Nightingale 2007), a central question is how (if at all) does top-down biosecurity governance need to change in response to synthetic biology?

Regulatory considerations of this kind are both familiar and new (Hamilton 2015). In the 1970s, recombinant DNA technology similarly emerged as a source of significant and contrasting expectations, and questions were posed about the

[1] In this chapter, 'top-down governance' is taken to mean laws, regulations, policies, guidelines and other government-led regulatory measures aimed at prohibiting undesirable behavior or encouraging desirable behavior on the part of countries, organizations or individuals engaged in aspects of the life sciences (research activities involving the use of biological materials, knowledge and/or technologies).

[2] In this chapter, 'biosecurity' is taken to mean measures aimed at preventing the *deliberate misuse* of the life sciences by non-state actors. In contrast, 'biosafety' is taken to mean measures aimed at preventing the *accidental or unintended misuse* of the life sciences.

suitability of existing regulatory approaches in light of potentially novel risks. However, in the case of recombinant DNA technology, biosafety concerns – notably, concens about the possible unintended consequences of genetically modified organisms (GMOs) – were the primary focus of scientific deliberations at the Asilomar Conference and subsequent policy discussions. In the case of synthetic biology, a field that has emerged at a time of heightened concerns about (bio)terrorism, the possibility that synthetic biology could enable non-state actors to acquire (novel) biological agents that could be used as weapons has been an omnipresent source of concern. In 2009, synthetic biology came to the attention of the US Federal Bureau of Investigation (FBI) and in 2016 gene editing was listed as a potential weapon of mass destruction (WMD) by the US Intelligence Community (Ledford 2010; Clapper 2016).

To more fully understand the top-down governance challenges introduced by synthetic biology it is necessary to consider how synthetic biology's novelties could disrupt or potentially undermine existing biosecurity regulations. In this chapter, we attempt to advance this discussion in several ways. First, we consider the scope and content of existing biosecurity regulations at the international and national levels. Second, we discuss several aspects of synthetic biology that present distinct regulatory challenges. Finally, we conclude with recommendations for strengthening current approaches to top-down biosecurity governance.

Taken together, we argue that although synthetic biology appears to be broadly (if indirectly) covered by existing international and national regulatory systems, several novelties underline the limitations of top-down governance approaches premised upon prohibiting access to specific 'intrinsically dangerous' scientific artifacts (McLeish and Nightingale 2007). Indeed, by some accounts, such restrictions may not only be ineffective, but may also make the world less safe. In an era of synthetic biology – characterized by technology convergence, increased access to bioengineering capabilities, and rapid growth in intangible life science knowledge – top-down governance must be increasingly adaptive, and hybrid forms of governance (incorporating a 'mix' of top-down and bottom-up approaches that leverage the self-governance potential of non-governmental actors) should be encouraged.

3.2 Understanding the Scope and Limitations of Top-Down Governance for Biosecurity and Synthetic Biology

To understand how synthetic biology could challenge or undermine existing approaches to biosecurity oversight and regulation, it is necessary to first consider the international legal instruments relevant to biosecurity, and how these instruments are implemented at the national level (Trump et al. 2020). Based on this analysis, it is apparent that there is no single international legal instrument and no 'one-size-fits-all' approach to national implementation. Rather, the regulatory space

governing biosecurity and synthetic biology can most accurately be described as a 'patchwork' of regulatory measures that tend to address biosecurity and synthetic biology indirectly. As scholars have previously observed, the regulatory space governing biosecurity comprises a "collection of cooperative and coercive national and international control measures – including international agreements, multinational organisations, national and international laws, regulations, policies, norms and rules – intended to prevent the spread of dangerous weapons and technologies" (McLeish and Nightingale 2007, p. 1638).

3.2.1 International Instruments for Biosecurity

3.2.1.1 Biological Weapons Convention (BWC)

International legal instruments establish global norms and obligations that are implemented by countries according to their unique risk and regulatory cultures. In relation to biosecurity, no single instrument is more important or directly relevant than the Convention on the Prohibition of the Development, Production, and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction, commonly known as the Biological Weapons Convention (BWC). The BWC, which opened for signature on 10 April 1972 and entered into force on 26 March 1975, is the first multilateral disarmament treaty banning the development, production and stockpiling of an entire category of WMD.[3] Under Article I of the Convention, member states agree that they must not "develop, produce, stockpile or otherwise acquire or retain: (1) Microbial 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; (2) Weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict."

Although tracing its origins to the Cold War, therefore focused on the activities of states and the possibility of biological warfare, the BWC remains relevant and has proven remarkably adaptive in the face of emerging concerns about non-state actors and advances in science and technology (S&T), including synthetic biology. In relation to non-state actors, the BWC requires, as defined under Article IV, States Parties to take any necessary measures "to prohibit and prevent the development, production, stockpiling, acquisition or retention of the agents, toxins, weapons, equipment and means of delivery specified in Article I of the Convention, within the territory of such state, under its jurisdiction or under its control anywhere." In other words, States Parties have a responsibility to enforce the Convention irrespective of who (state or non-state) is acting in contravention to the universal ban on biological weapons.

[3] See: https://www.un.org/disarmament/wmd/bio/

In relation to advances in S&T, the BWC is widely recognized as embodying a 'General Purpose Criterion', whereby the hostile use of biology – irrespective of the specific agents, knowledge or technologies involved – is universally prohibited. This means that new discoveries enabled by advances in S&T, including possible future 'novel' agents produced using synthetic biology techniques or technologies, are covered (Hart and Trapp 2012). In other words, the BWC is effectively 'future proofed' – it "cannot be innovated around, and it embodies the norm in a timeless form" (McLeish and Nightingale 2007, p. 1638).

With a view to advances in synthetic biology, States Parties to the BWC recognize that the field, among other areas of S&T, is rapidly evolving and could potentially introduce novel risks over time (Hart and Trapp 2012). It is equally recognized that developments in S&T could offer new opportunities for countering bioterrorism, and detecting and responding to attacks should they occur (ibid.). To keep pace with advances in S&T and their implications for the BWC, there is general support among States Parties for increased scientific and technical review within the BWC process (ibid.). Notably, proposals have been made for establishing a scientific advisory body that could play a critical role in assessing the impact of advances in S&T on the BWC regime, as well as building consensus among States Parties based on a systematic review of developments in the life sciences relevant to the Convention (ibid.).

While the BWC establishes a global norm against the hostile use of biology, it is nonetheless confronted by a number of challenges and limitations. Notably, despite having 183 States Parties, four Signatory States have yet to ratify the Convention, and ten states have neither signed nor ratified it. There is therefore a need to continue to strive for universality to ensure that the BWC is universally ascribed to and ultimately implemented and enforced at the national level. Moreover, the BWC lacks a verification mechanism to monitor compliance with the Convention. In the absence of such a mechanism, confidence-building measures (CBMs) – voluntary annual reports describing a member state's activities relevant to the Convention – are intended to build trust and transparency. However, annual CBM submissions remain low, the quality of submissions is inconsistent, and States Parties are not obliged to explicitly report on S&T developments (Lentzos and Hamilton 2010). Finally, the BWC is limited by resource constraints and currently depends upon a three-person team – the BWC Implementation Support Unit (ISU) – to facilitate meetings and support daily administrative operations (Hart and Trapp 2012).

3.2.1.2 Chemical Weapons Convention (CWC)

Complementing the BWC, the Convention on the Prohibition of the Development, Production, Stockpiling, and Use of Chemical Weapons and on their Destruction, commonly known as the Chemical Weapons Convention (CWC), prohibits the development, acquisition, possession, transfer and use of toxic chemicals and their precursors for weapons purposes. Unlike the BWC, the CWC, which opened for signature in 1993 and entered into force four years later, is administered by an

autonomous international organization, the Organization for the Prohibition of Chemical Weapons (OPCW), which performs a variety of administrative, legal and field functions, including verification to ensure compliance.

Because the BWC and CWC both cover toxins, there exists an overlap between the two conventions and the possibility of mutually reinforcing legal coverage (Hart and Trapp 2012). However, because toxins can be interpreted as biological *or* chemical weapons, situations could arise where states decline to take specific measures to prevent the misuse of toxins under either agreement (ibid.). Advances in synthetic biology – an interdisciplinary field encompassing biology, chemistry, engineering and computing – are likely to make distinctions between chemical and biological weapons even more complex. In this environment, there is a need for inter-convention dialogue to better understand the risks, as well as the jurisdictions and responsibilities of all relevant international conventions and legal instruments.

3.2.1.3 Australia Group, United Nations Security Council Resolution 1540 and Others

Other important international instruments relevant to biosecurity include the Australia Group (AG) and United Nations Security Council Resolution 1540 (UNSCR 1540). In the case of the AG, established in 1985 in response to evidence that Iraq had sourced precursor chemicals and materials for its chemical warfare program through legitimate channels,[4] member states have harmonized export controls covering materials and technologies likely to contribute to the development of chemical or biological weapons. Biological agents and dual-use biotechnology were specifically added to the AG guidelines in 1992 (Oye 2012). In 2008, in light of advances in synthetic biology, the AG established a dedicated advisory body to keep pace with developments in the field and to suggest responses to synthetic biology innovations (ibid.). A key challenge faced by the AG is the growing relevance of intangible technology transfers, which not only make-up an increasingly significant component of legitimate life science research, but also present distinct challenges to regulatory control. Unlike physical pathogens and dual-use equipment, intangible life science transfers cannot be easily monitored and prevented from crossing borders. In the case of synthetic biology, a field characterized as much by digital and informational resources (e.g. DNA sequence information) as physical ones (e.g. DNA sequencers), the regulatory challenges posed by intangible technology transfers are especially acute.

Established in 2004, UNSCR 1540 "obliges States, *inter alia*, to refrain from supporting by any means non-State actors from developing, acquiring, manufacturing, possessing, transporting, transferring or using nuclear, chemical or biological

[4] See 'the origins of the Australia Group'. The Australia Group website. URL [https://www.dfat.gov.au/publications/minisite/theaustraliagroupnet/site/en/origins.html] (accessed 25 March 2021)

weapons and their means of delivery."[5] Under this resolution, member states have specifically agreed to enact relevant legislation and to demonstrate national implementation through national reporting. In addition to directly contributing to global efforts to combat WMD, UNSCR 1540 is significant due to its explicit focus on non-state actors. This focus, as others have observed, "marks a new development in biosecurity policy, which historically has been state-centric" (McLeish and Nightingale 2007, p. 1640). This development not only reflects growing concerns about bioterrorism, but also the belief that advances in S&T have contributed to lowering technical barriers and enhancing the capabilities of non-state actors (ibid.).

In addition to the international instruments discussed above, further international regulations and conventions, including the World Health Organization (WHO) International Health Regulations (2005) (IHR) and the Convention on Biological Diversity (CBD), cover aspects of biosecurity and synthetic biology. In the case of the IHR, the scope of the regulations cover natural, accidental and deliberate disease events, thus capturing biosafety and biosecurity. The WHO, which directs and coordinates international health within the UN system, also monitors and offers guidance on life science research recognized as dual-use research of concern (DURC), including notable experiments involving synthetic biology. In 2012, in response to two such experiments (one led by a team in the Netherlands, the other by a team in the US) that resulted in laboratory-modified H5N1 viruses capable of airborne transmission between mammals ('gain-of-function' experiments), the WHO convened a technical advisory group that considered the biosafety and biosecurity implications of the research, including concerns about the public dissemination of the findings (WHO 2012). In 2015, the WHO convened another scientific working group to address the public health implications of synthetic biology as it relates to smallpox preparedness and control (WHO 2015). The working group concluded that, in light of advances in synthetic biology, including *de novo* DNA synthesis, the risk of smallpox re-emerging can never be fully eradicated. Among the working group's recommendations was the need for revised regulations for research on DNA fragments and the synthesis of virus DNA by new technological approaches.

In the case of the CBD, many considerations that apply to GMOs remain relevant in the case of synthetic biology. Since 2010, the CBD has considered whether synthetic biology should be classified as a new field presenting novel risks and whether new regulations are needed in view of the protection of biodiversity and genetic resources (Lai et al. 2019). Although these deliberations have been oriented to biosafety, the protection of biodiversity and the management of digital sequence information are also relevant for biosecurity.

Taken together, these international conventions and agreements create overlapping governance structures that cover biosecurity and synthetic biology more or less directly. Over time, each of these conventions have evolved and adapted to address emerging risks and regulatory challenges introduced by advances in S&T and non-state actors. As they will undoubtedly continue to evolve and adapt, it will be

[5] See: https://www.un.org/en/sc/1540/about-1540-committee/general-information.shtml

important for all parties to monitor developments in synthetic biology, develop and share common definitions, and determine to what extent synthetic biology introduces novel biosafety and biosecurity risks.

3.2.2 National Implementation

International conventions are intent-based, broadly defined and therefore generally future proofed, but they only take effect when they are ratified and implemented at the national level. For example, to implement the BWC, countries must adopt appropriate penal measures criminalizing the production, handling and use of biological weapons;[6] biosafety and biosecurity measures accounting for the safe and secure handling of dangerous pathogens; and import and export controls covering specific biological agents and dual-use equipment and technology.[7] Finally, enforcement measures must be adopted to ensure the ongoing monitoring of life science activity and to prosecute and punish offenders.[8] How countries carry out each of these implementation measures is influenced by a variety of factors, including a country's attitudes toward risk and the importance of technological innovation. In practice, countries often draw on and/or adapt existing laws and regulations, rather than creating new ones. For example, aspects of the BWC may already be covered by existing criminal laws, public health (and medical) laws, emergency management laws and/or national security laws (Fidler 2001; Colussi 2015). This means that national implementation not only takes different forms *between* countries, but also tends to result in a patchwork of rules applying directly, or more often indirectly, to biosecurity and synthetic biology *within* countries.

With a view to national implementation, this section discusses some general characteristics of top-down approaches to biosecurity and synthetic biology regulation. There are numerous categorizations that can be used to group these approaches, but for the purpose of this chapter we limit ourselves to the distinction between hard and soft law, between different levels of precaution in governance, and between general and specific legislation. It should be emphasized that these distinctions are merely ideal types. While some examples of national implementation will be given, it should be noted that most countries apply a mix of different strategies that cannot be strictly assigned to a single type of governance.

[6] See for example The Biological Weapons Act (1974) in The UK or the Biological Weapons Act (1989) in the USA.

[7] See VERTIC factsheet on national implementation measures for the BWC, available at: http://www.vertic.org/wp-content/uploads/2019/08/FS7_BWC_EN_FEB_2018.pdf

[8] Ibid.

3.2.2.1 Hard Law vs. Soft Law

When selecting regulatory options, national governments have to balance *hard law*, meaning statutorily defined legal prescriptions that result in punishment when violated, and *soft law*, comprised of norms and standards within the operating community that build validity, trust, and collaboration opportunities between community members and other stakeholders. By these definitions, hard law is generally taken to correlate with traditional 'top-down' governance. However, a government can equally make the deliberate 'top-down' choice to cede some responsibility to soft law in an effort to stimulate ownership and self-responsibility on the part of industry and technology users, encourage economic development, limit the burden and costs of regulatory oversight, etc. (Palumbo and Bellamy 2010). The balancing of hard and soft law can be categorized according to three generalized types of governance approach: precautionary, laissez-faire and stewardship (Linkov et al. 2018a, b).

Precautionary Governance

There is a broad range of precautionary approaches that are discussed in the scholarly literature and that have been implemented by governments in practice (Ahteensuu and Sandin 2012; Dinneen 2013). Rather than analyzing each of these approaches in detail, the following discussion considers precautionary governance more generally, treating it as a set of pre-emptive regulations aimed at ensuring the safe and secure application of technologies and preventing exposure to risk (Linkov et al. 2018a, b).

In general, precautionary governance is associated with risk-aversion and centralized governance systems that require safety to be demonstrated prior to permitting the use of new technologies or products (Stirling 2006). For example, the European Union (EU) is widely known to take a precautionary approach in relation to GMO biosafety as prescribed by EU legislation (European Commission 2000; Anyshchenko 2019). This legislation, which aims to protect the health and safety of humans, animals, and the environment from adverse biological contamination, equally applies to aspects of synthetic biology (especially genome editing).[9]

Comparable legal requirements for biosecurity were introduced later in Europe (2000),[10] and much of the GMO debate remains focused on the subject of biosafety. Following a recent review process on whether or not existing gene technology regulations and risk assessment and management practices are applicable to synthetic biology, three opinion statements by the Scientific Committees did not address

[9] See Case C-528/16, Court of Justice of the European Union 2018. Organisms obtained by mutagenesis are GMOs and are, in principle, subject to the obligations laid down by the GMO Directive. However, whereas radiation and chemically induced mutagenesis are exempt from the regulations because they have a so called 'history of safe use', mutagenesis induced by gene editing techniques such as CRISPR is not because it lacks this 'history of safe use'.

[10] See Regulation 1334/2000 of 22nd June 2000 setting up a Community regime for the control of exports of dual-use items and technology in O.J. L 159/2000, modified by Regulation 2432/2001 of 20th November 2001 in O.J. L 338/2001, and by Regulation 428/2009 of 5th May 2009 in O.J. L 134/2009.

biosecurity directly, focusing solely on biosafety (SCHER, SCENIHR and SCCS 2014; SCENIHR, SCHER and SCCS 2015). By contrast, synthetic biology's biosecurity implications [11] have been the subject of considerably more policy discussion in the US (e.g. NSABB 2006, 2011; for a review, see Oye 2012). Whereas Europe has historically strongly focused on biosafety, biosecurity regulations were developed in the US at a relatively early stage (1989). Moreover, since 9/11 and the subsequent anthrax letter attacks, US policy has further emphasized biosecurity (McCarty 2018). These developments have resulted in extensive controls on scientific research (McLeish and Nightingale 2007).[12]

A precautionary governance system seeks to protect against undue and unnecessary harm, but this approach can also impose costs. It is often argued that a strict pre-emptive regulatory system can potentially cut off avenues for innovation and industry and diminish a country's economic development and international competitiveness. These potential pitfalls have been pointed out both in relation to GMO biosafety regulations in Europe and biosecurity controls in the US (Wager and McHughen 2010; Bogner and Torgersen 2018; Gaudioso and Salerno 2004). Moreover, in a world where other countries may be more risk-tolerant, countries that adopt a precautionary governance approach are not necessarily insulated from risk. This problem has been faced before when individual countries have pursued, for example, nuclear disarmament or sought to reduce or eliminate nuclear power plants domestically while neighbors have not. Thus, strict adherence to precautionary governance in the case of biosecurity and synthetic biology is not a panacea for all threats.

Laissez-Faire Governance

A laissez-faire governance approach cedes much of the regulatory power to existing or emerging bottom-up initiatives, placing trust in the capacity of technology producers, industry and users to play an active role in their own regulation. Under this approach, such non-governmental actors are encouraged to determine (at least in part) how safety and security practices are structured, implemented and enforced, while centralized government plays a role in setting minimum standards and intervening in the event of regulatory failures. This approach is generally intended to promote innovation and flexibility, as well as rapid adaption and response to emerging threats (Linkov et al. 2018a, b).

While laissez-faire governance is a promising approach that recognizes the important role that non-governmental actors can play in the regulatory process, there are also potential pitfalls. One such example, albeit focused on bioethics rather than biosecurity, can be traced to the use of germline editing in humans to produce the first CRISPR baby. In this case, despite broad international agreement that scientists should *"hold off on editing human eggs, sperm or embryos until gene-editing*

[11] See Ahteensuu 2017.

[12] For a review of all the legislative framework about bioterrorism in the U.S.A., see RICHARDS, Edward P./O'Brien, Terry/Ratburn, Katharine C., "Bioterrorism and the Use of Fear in Public Health", The Urban Lawyer, No. 3, Vol. 34, 2002, pp. 685–726.

technology (and the implications of the edits) are better understood."[13] (See also Cyranoski and Ledford 2018), a researcher in China took advantage of laissez-faire regulatory controls that resulted in multiple potential risks and unintended consequences. These included the possibility of long-term changes to the human germline; encouraging other scientists (including those working internationally) to pursue germline editing in humans (Cyranoski 2019a, b), and motivating Chinese regulators to introduce stricter regulatory controls on genetic research (ibid.).

As the above example suggests, one risk of laissez-faire governance is that an individual's risk tolerance may not (intentionally or unintentionally) conform to existing norms and their actions may subsequently expose everyone to undue risk or irreversible harm, with implications for the laissez-faire state as well as other states. Additionally, the more a state relies on soft law, the more responsibility the government delegates to individuals, groups and organizations, not only to establish norms and follow them, but also to enforce them. In the case of synthetic biology, such bottom-up initiatives have played an important role in this rapidly developing field. Organizations such as the International Gene Synthesis Consortium (IGSC) have come to play an important role in the regulatory process by, for example, developing industry standards and guidelines (IGSC 2017). For better or worse, the success of such approaches will depend on the commitment of non-governmental actors to act in the best interests of society, valuing safety and security as a public good.

Ultimately, while a laissez-faire approach may effectively supplement aspects of centralized government regulation, it cannot be expected to fully replace it. This is because, as history has shown, individual researchers or individual members of industry will sometimes choose to value personal prestige or cost cutting over safety and security. Moreover, from the standpoint of non-governmental actors, including the DNA synthesis consortia noted above, regulation is not necessarily a bad thing. Indeed, by some accounts, the standards and codes of conduct produced by the DNA synthesis industry were motivated by a lack of top-down regulations that could provide a benchmark for not only mitigating potential biosecurity risks, but also liability issues and reputational costs in the event of an incident. For this reason, the US Government's own DNA screening guidance[14] has been largely welcomed by industry.

Stewardship Governance

A stewardship governance approach seeks to balance the advantages of laissez-faire governance with centralized risk management, and different countries may enact stewardship approaches that incline towards one side or the other (Linkov et al. 2018a, b). Governments that adopt a stewardship governance approach to synthetic

[13] Many articles and newspaper items have in response to the Jiankui He case referred to the (perceived) broad worldwide consensus that germline editing in the clinic would be a step too far. See a.o. Weintraub (2019).

[14] See: https://www.phe.gov/Preparedness/legal/guidance/syndna/Documents/syndna-guidance.pdf

biology will seek to monitor developments in the field, enabling space for innovators and industry to operate, while intervening in the event of observed inconsistencies with objectives formulated through multi-stakeholder processes involving both government and non-governmental actors. Stewardship governance is more guidance than direction, and typically involves the active participation of bottom-up entities in formulating norms alongside traditional top-down regulatory bodies. Though some hard constraints exist, they are likely to arise through consensus driven collaborative forums that both support beneficial innovation and use of technologies while critically evaluating risks (the Goldilocks principle).

Many countries apply a stewardship style of governance for emerging technologies, including synthetic biology. While the specific approaches of individual countries differ at the level of detail, they are all based on the principles of being flexible and adaptive and using a mix of different tools to achieve a 'balanced' form of governance. For example, the US employs a stewardship model in much of its engagement with emerging technology developers and users: the executive government, state governments, the US patent system, insurers, and the system of legal liability all serve to foster innovation while constraining what scientists can attempt within established risk tolerances. The stewardship model aims to limit innovation only when the risks are deemed sufficient to justify government intervention.

Similar governance concepts, capturing the notion of balancing laissez-faire and precautionary models, mentioned in the literature include 'adaptive governance' and 'prudent vigilance'. The main characteristic of adaptive governance is its emphasis on flexibility, allowing "stakeholders in industry, government, and society at large to iteratively adjust their best practices and codes of conduct to derive the benefits…without incurring unnecessary or unacceptable risks or losses" (Linkov et al. 2018a, b). The 'prudent vigilance' model "establish[es] processes for assessing likely benefits along with safety and security risks both before and after projects are undertaken" (PCBSI 2010). Introduced by the US Presidential Commission for the Study of Bioethical Issues in its policy report on synthetic biology, the model reflects a combination of 'top-down' and 'bottom-up' strategies for the enforcement and control of biosecurity risks associated with synthetic biology (see Collussi 2015).

3.2.2.2 Biosafety vs. Biosecurity, GMOs vs. Synthetic Biology

Given that biosecurity and synthetic biology are relatively new concepts with limited regulatory legacies, there are few sign posts to indicate how countries' regulatory frameworks should evolve to meet their associated risks, and even if new regulations are needed. In light of existing GMO and biosafety regulations, countries are faced with the question of determining what is already covered and what is not. In this context, much depends on the 'newness' or 'novelty' ascribed to synthetic biology relative to conventional biotechnology, and governments must weigh the benefits and costs of introducing new regulations that are typically complex and time-consuming to produce (Hamilton 2015).

Even in states where synthetic biology is actively pursued, many do not (yet) explicitly reference it in legal documentation. In Germany, for example, the Research Office of Parliament concluded in 2015 that the processes currently called 'synthetic biology' are in fact still conventional biotechnology and can be covered by existing regulations, including existing security, transport, and export control regulations, and the Health Care Act, for issues related to human health. From the standpoint of the Research Office of Parliament, synthetic biology results in new genetic combinations of a host organism with a variable amount of new genetic material, just like GMOs. Similar conclusions have been reached by scientific advisory bodies in Europe and beyond (Trump 2017; ZKBS 2018; Pauwels et al. 2013).

Synthetic biology is similarly not mentioned in EU legislation and, historically, changes to the EU biosafety regulations have proven to be extremely time consuming due to different perspectives on both the necessity and desirability of change (Eriksson et al. 2018). In the case of several new plant breeding techniques, it remains unclear whether they are covered by EU GMO legislation, despite deliberations (including several scientific and legal expert committees and reports) stretching back more than 15 years.

Finally, distinctions between biosecurity and biosafety can be ambiguous. In countries with regulations specifically covering biosecurity, a variety of definitions can be found depending on the context and field of application. For example, different interpretations exist between the human health sector, and the animal and plant health sectors . In the case of human health, biosecurity is generally understood as a set of regulatory measures aimed at preventing the deliberate misuse of biology (i.e. the same way we interpret biosecurity in this chapter). In the case of animal and plant health, biosecurity is generally understood as a set of regulatory measures aimed at preventing and responding to the natural or unintentional introduction, establishment and spread of pests or pathogens (Mumford et al. 2017).[15] Some languages also lack distinct words for biosafety and biosecurity (at least in general usage). For example, *biosecuridad,* in Spanish, *Biosicherheit,* in German, and *bioturvallisuus,* in Finnish, are generally used to capture both biosafety and biosecurity. This can result in misunderstandings, as these concepts can be understood differently between countries and between sectors. In the case of languages that do differentiate between biosafety and biosecurity, there can nonetheless be confusion

[15] In the setting of the BWC, it is most commonly used to refer to mechanisms to establish and maintain the security and oversight of pathogenic microorganisms, toxins and relevant resources. But For example, the glossary of the FAO Basic Laboratory Manual for the Small-Scale Production and Testing of I-2 Newcastle Disease Vaccine considers biosecurity to be "precautions taken to minimize the risk of introducing an infectious agent into a population". And in the glossary of the New Zealand Parliamentary Commissioner for the Environment considers biosecurity to be "The exclusion, eradication and effective management of pests and unwanted organisms into New Zealand." http://www.pce.govt.nz/reports/pce_reports_glossary.shtml. The OECD developed best practice guidelines for biosecurity at ancillary facilities, defining it as "institutional and personal security measures and procedures designed to prevent the loss, theft, misuse, diversion or intentional release of pathogens, or parts of them, and toxin-producing organisms, as well as such toxins that are held, transferred and/or supplied by Biological Resource Centres".

over how each set of practices should be applied and what actors or institutions bear responsibility for their oversight. Recognizing these ambiguities, initiatives in the EU and Central Asia have been undertaken to map how these terms are understood and applied in different countries (EBRF 2016; EEAS 2017).

3.2.2.3 National Implementation: An Inevitable Patchwork

In many (if not most) countries, the regulatory frameworks governing synthetic biology and biosecurity are fragmented – divided across multiple pieces of legislation (e.g. legislation on bioweapons, dual-use materials and technologies; export/import and transport; gene technology; human health; microorganisms, animal and plant health; agriculture; occupational health; waste disposal; criminal behavior, etc.) – and tend to address one or both subjects only indirectly (Greer and Trump 2019). In Finland, for example, over twenty acts and regulations can be interpreted as governing the biosafety and biosecurity dimensions of synthetic biology, and none make explicit reference to 'synthetic biology'. In other countries, like the US, synthetic biology is explicitly referenced in relevant regulations and guidance documents (e.g. federal DNA screening guidance), accompanied by more than 35 different biosecurity regulations (some of which have been described as mutually inconsistent, making compliance with all of them impossible): "The regulation of products of synthetic biology is juggled, and not always clearly so, among three federal agencies, various federal laws, and the Coordinated Framework (…). The regulatory framework that has evolved is complicated, increasingly circuitous, and not for the faint of heart" (Bergeson et al. 2015).

In other countries, especially developing countries that may share very different priorities due to limited resources and urgent challenges associated with human rights and food security, relevant biosecurity and synthetic biology regulations have not yet been adopted. Thus, the fact that international conventions are in place may create a false sense of confidence about the level of consensus and adoption. In practice, the effectiveness of conventions depends on how they are implemented, a task that can take a considerable amount of time. Indeed, despite the relatively long history of GMO regulation, relevant laws have not been adopted by all countries.

Additionally, in an interconnected and globalized world, the effectiveness of national implementation is limited in its ability to prevent or limit access to new technologies that may be carelessly used or transferred by other states. National implementation acts within legal and geographical boundaries and depends upon rules designed to shape the behavior of domestic audiences. For truly robust governance to occur, all states must work to mitigate the risks posed by advances in synthetic biology through effective national implementation.

Given the diversity of national implementation efforts globally, it seems unlikely that there will be a unified approach and that all gaps in the governance of synthetic biology will be filled. However, potential vulnerabilities can be addressed through a combination of different instruments. "Often, approaches to risk governance are defined in terms of a choice between two alternatives. Either accept the

precautionary principle but in so doing choke off development of potentially promising technologies, or go with laissez-faire and in so doing accept potentially irreversible harms" (Oye 2012, p. 22). Linkov, Trump, Poinsatte-Jones, and Florin (2018b) emphasize the importance of a stepwise learning approach under conditions of acknowledged uncertainty, with initial limits on use, iterative phases of data gathering and regulatory evaluation. In addition to adopting hybrid governance models, combining elements of precaution with policies aimed at stimulating innovation, governments may also look to strengthen regulatory systems through a combination of hard and soft law. For example, legal measures can be complemented by codes of conduct or guidelines produced by researchers and industry.

Top-down governance systems, in their various forms, offer advantages and disadvantages. The regulatory challenges presented by synthetic biology will require the careful consideration of multiple (hybrid) governance options.

3.3 Key Novelties and Tensions Introduced by Synthetic Biology

Biosecurity in the context of synthetic biology benefits from the groundwork previously laid to mitigate biological weapons threats and the risks posed by earlier advances in biotechnology. We have seen that international conventions and national implementation already cover (albeit imperfectly) many aspects of synthetic biology. In this section, we discuss three aspects of synthetic biology that represent distinct governance challenges: convergence, democratization and intangibility. Cutting across these tensions are overarching issues that are familiar to all emerging technology discussions, including the pace of technological change and uncertainty, both in terms of the potential risks and benefits (Marchant et al. 2011). For effective governance in this environment, regulatory efforts must seek to be forward-looking and adaptive. Moreover, whether states are applying existing legislation to synthetic biology or enacting new legislation, both relevance and coherence will be paramount.

3.3.1 Convergence

Because synthetic biology represents a convergence between biology, chemistry, engineering and computing, ambiguities may arise regarding which conventions should regulate specific developments. This could produce redundancies in regulatory efforts or, far worse, gaps in responsibility as each authority presumes another's attention and jurisdiction. Frontier research on protocells and xenobiology, among other domains of synthetic biology that push the limits of scientific classification, may even fall outside the scope or remit of existing conventions and established legislation. Other synthetic biology risks, including those that blur the line between

biological and informational hazards, may require new security concepts and practices. For example, recent studies that have demonstrated the capacity to encode computer viruses in synthesized strands of DNA, exploiting vulnerabilities in the sequencing and processing pipeline (Ney et al. 2017), underline the growing relevance of *cyberbiosecurity*, an emerging field at the intersection of cybersecurity and biosecurity.

Synthetic biology processes and methods may also become (or may already *be*) too diverse to legislate individually, and the convergent nature of synthetic biology may lead to fragmentation or duplication of laws at the national level. In this environment, it may become increasingly unclear which laws should be applied to synthetic biology and how judges or legislators should interpret and apply them. In light of its numerous applications, multiple contributing scientific disciplines, and practitioners working in both institutional and non-institutional settings, synthetic biology is an exemplary case of convergence.

3.3.2 Democratization

Synthetic biology provides new ways to modify organisms outside of dedicated laboratories and without advanced skills (Oye 2012). This broadens access to the science and enables individuals to apply its techniques without oversight from formal institutions or associated institutional norms (NSABB 2011; Gruber 2019). Theoretically, democratization could allow untrained or malicious actors to create dangerous organisms. In practice, current synthetic biology applications are far from facilitating this: in most cases, so-called do-it-yourself (DIY) biology is limited to relatively simple experiments with nonpathogenic organisms, with relatively low success rates (Kuiken 2016). However, looking to the future, it is possible that advances in synthetic biology will lower the technical barriers needed to engage in more advanced bioengineering projects. Much like the history of computing, as synthetic biology tools and techniques become more reliable, streamlined, and easy to use, bioengineering may become common place, accessible to specialists and non-specialists alike.

If synthetic biology does (eventually) make biology easy or at least significantly *easier* to engineer, traditional top-down governance and enforcement will no longer be sufficient to provide adequate oversight, and there is likely to be a growing need to enlist the support of the synthetic biology community itself to participate in various forms of self-regulation or self-policing. Already, innovative self-governance approaches of this kind have been employed in the context of DIY-biology, wherein DIY-culture and social protocols have been leveraged to support responsible science and self-regulation (Bolton and Thomas 2014). However, such regulation works only if all parties engage, or are permitted to engage, which is not always guaranteed.

One potential model for policing synthetic biology in an era of democratization is provided by the partnership that has evolved between the International Genetically Engineered Machine (iGEM) competition and the US FBI. This partnership has

sought to create a culture of trust and transparency between law enforcement and members of the synthetic biology community through engagement with students and the private sector, demonstrating positive results (Ossola 2016). Moreover, iGEM organizers require, as a condition of student teams' participation, students to engage with safety and security issues throughout their projects (Oye 2012). These partnership activities create an opportunity for mutual learning, but there can be tensions. In 2019, 47 countries sent teams to iGEM, but some international students were barred from attending the event (Baber 2018) due to a US Executive Order that banned students from several countries, including Iran and Syria. This represented a collision of top-down priorities. The travel ban's focus on national security compromised the FBI's ability to build relationships within the evolving international synthetic biology community.

Democratization in synthetic biology requires balancing individual liberty and risk prevention. In a hypothetical future world of broad bioengineering capabilities, safeguards will still be necessary, but whether they are best applied through top-down or bottom-up efforts remains to be seen. The successful governance of synthetic biology will partially depend upon the functioning collaboration between top-down and bottom-up governance in identifying and preventing purposeful or accidental misuse. Bottom-up governance is further discussed in Chap. 6 of this volume.

3.3.3 Intangibility

The 'ingredients' for synthetic biology are increasingly informational, thus regulations focusing on material control, while important, cannot address the full scope of synthetic biology's risks. Digital sequence information, access to online research protocols and methodologies, and the capacity to construct laboratory hardware from scratch using 3D-printing technologies are all developments that threaten to undermine regulatory systems that privilege policies aimed at restricting access to physical technologies (NRC 2004). In an era of the life sciences dominated by the production and distribution of information-based resources, effective regulatory controls on intangible technology transfers are essential. However, successfully designing and implementing controls of this kind is a challenging task. Whereas dual-use equipment must (or at least should) pass through physical checkpoints, digital sequence information can be transmitted with the click of a button.

Advances in synthetic biology may also yield threats that are not only difficult to regulate, but impossible to *anticipate*. For example, it may someday be possible to design and build novel genomes (based on existing, modified or new genetic code) that transcribe previously unknown pathogens. Therefore, although select agent lists are likely to remain relevant (if for no other reason than because they generate awareness about pathogens that *are known* to cause severe harm to public, animal or plant health), they cannot be expected to capture the full spectrum of harmful agents that are (or may someday be) possible to create.

Finally, in the context of synthetic biology and the contemporary life sciences in general, important questions remain about what life science information should be considered 'risky' in the first place and how this information aught to be controlled. To place these considerations in context, one need look no further than the H5N1 gain-of-function experiments (Imai et al. 2012). In this case, concerns were raised about whether research describing the synthesis of a novel H5N1 variant was suitable for open publication. Some argued publishing the protocols would provide a blueprint for bioterrorism. Others asserted that the research should never have been conducted. Decisions about whether (or what parts of) the research should be published were sources of international debate and global controversy (Hamilton 2015). While past technologies have motivated similar controversies (see McLeish and Nightingale 2007), questions about the intrinsic dangers of life science information, and what information may be too dangerous to share, have never been more acute.

3.4 Conclusions and Recommendations

- The regulatory landscape for biosecurity and synthetic biology can best be described as a 'patchwork' of international conventions, national laws, regulations, guidelines, etc. In many instances, these were designed to address other (state biowarfare programs) or earlier (biosafety) concerns.
- While synthetic biology appears to be broadly (if indirectly) covered by existing top-down governance measures (e.g. GMO laws), several characteristics of the science, including convergence, democratization and intangibility, point to possible regulatory gaps. How governments address these novelties depends upon their regulatory cultures and perceptions of risk.
- To date, the regulatory response, while varied (ranging from more precautionary to more laissez-faire), suggests a preference for evolutionary rather that revolutionary regulatory change. Like the regulatory response to GMOs, there is a tendency for governments to adapt existing regulations to new technologies.
- Whether new conventions, laws or regulations are (or are not) needed to address synthetic biology's novelties is open to question. At the very least, there is a need to monitor advances in the field and to consider how top-down governance approaches could be improved. The following recommendations aim to advance this discussion:
- The BWC, the premier international forum that addresses biological threats, should play a leading role in monitoring security-relevant advances in synthetic biology. Proposals to establish a BWC scientific advisory body and to introduce a S&T reporting requirement into the CBM mechanism should be encouraged.
- In view of the growing convergence between biology, chemistry, engineering and computing, inter-convention dialogue is needed between the BWC and CWC, among others, to ensure the full scope of synthetic biology's risks are taken into consideration and that there is agreement on how to address these risks in the event of deliberate misuse by state or non-state actors.

- Given that many security concerns about synthetic biology relate to its informational (e.g. digital sequence information) rather than physical (e.g. DNA sequencers) dimensions, it is necessary to develop improved methods of regulating intangible technology transfers. It is no longer sufficient to rely exclusively on material controls and list-based approaches to regulation.
- Synthetic biology is contributing to the democratization of genetic engineering. It is therefore essential to enlist the support of non-governmental organizations and actors, including technology developers, industry and users, in the regulatory response. The value of complementing top-down governance measures with bottom-up governance measures, drawing on limited forms of self-regulation or self-policing, will only increase as the tools of modern biology become more accessible.
- There is no one-size-fits-all approach to synthetic biology's governance. Finding the appropriate 'mix' of top-down and bottom-up regulatory measures will require foresight, broad dialogue, and a willingness on the part of governments to look to new, hybrid forms of risk regulation.

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References

Ahteensuu M (2017) Synthetic biology, genome editing, and the risk of bioterrorism. Sci Eng Ethics 23(6):1541–1561

Ahteensuu M, Sandin P (2012) The precautionary principle. In: Hillerbrand R, Sandin P, Roeser S, Peterson M (eds) Handbook of risk theory: epistemology, decision theory, ethics and social implications of risk. Springer Netherlands, Dordrecht, pp 961–978

Anyshchenko A (2019) The precautionary principle in EU regulation of GMOs: socio-economic considerations and ethical implications of biotechnology. J Agric Environ Ethics 32(5–6):855–872

Baber S (2018) Visa issues prevent several international students from attending iGEM Giant Jamboree. The Tech, 8 November 2018. Available: https://thetech.com/2018/11/08/igem-competition-students. Last accessed 26 Sept 2019

Bergeson LL et al (2015) The DNA of the U.S. Regulatory system: are we getting it right for synthetic biology. Woodrow Wilson Center, October 2015

Bogner A, Torgersen H (2018) Precaution, responsible innovation and beyond–in search of a sustainable agricultural biotechnology policy. Front Plant Sci 9:1884

Bolton R, Thomas R (2014) Biohackers: the science, politics, and economics of synthetic biology. Innov Technol Govern Global 9(1–2): 213–219
Cello J, Paul AV, Wimmer E (2002) Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template. Science 297(5583):1016–1018
Clapper JR (2016) Worldwide threat assessment of the US Intelligence Community. Statement for the Record. Senate Armed Services Committee, 9 February 2016. https://www.dni.gov/files/documents/SASC_Unclassified_2016_ATA_SFR_FINAL.pdf
Colussi IA (2015) Synthetic biology as a new threat to biosecurity. Is there a road to suitable governance? Bioterrorismo y bioseguridad 65–110
Cyranoski D (2019a) China set to introduce gene-editing regulation following CRISPR-baby furore. Nature, 21 May 2019
Cyranoski D (2019b) Russian 'CRISPR-baby' scientist has started editing genes in human eggs with goal of altering deaf gene. Nature News, 18 October 2019
Cyranoski D, Ledford H (2018) Genome-edited baby claim provokes international outcry. Nature 563(7733):607–608
Dinneen N (2013) Precautionary discourse. Politics Life Sci 32(1):2–21
Endy D (2005) Foundations for engineering biology. Nature 438(24):449–453
Eriksson D et al (2018) A welcome proposal to amend the GMO legislation of the EU. Sci Soc 36(11):1100–1103. https://doi.org/10.1016/j.tibtech.2018.05.001
European Biosecurity Regulators Forum (2016) Securing immaterial technology with dual-use potential (working paper). http://www.ebrf.eu/documents.html
European Commission (2000) Communication from the Commission on the precautionary principle/*COM/2000/0001 final*/, 8 See also: https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A52000DC0001
European External Action Service (2017) EU funded project on biosafety and biosecurity kicks-Off regionally in Central Asia. Press release 02/02/2017. UNIQUE ID: 170202_11
Fidler DP (2001) The globalization of public health: the first 100 years of international health diplomacy. Bullet World Health Organ 79:842–849
Garfinkel MS, Endy D, Epstein GL, Friedman RM (2007) Synthetic genomics: options for governance. Available at: http://www.jcvi.org/
Gaudioso J, Salerno RM (2004) Biosecurity and research: minimizing adverse impacts. Science 304(5671):687–687
Greer SL, Trump B (2019) Regulation and regime: the comparative politics of adaptive regulation in synthetic biology. Policy Sci 52(4):505–524
Gruber K (2019) Biohackers: a growing number of amateurs join the do-it-yourself molecular biology movement outside academic laboratories. EMBO Rep 20(6):e48397
Hamilton RA (2015) Governing through risk: synthetic biology and the risk management process. PhD thesis, The London School of Economics and Political Science (LSE)
Hart J, Trapp R (2012) Science, technology, and the biological weapons convention. Arms Control Today 42(8):15–21
Imai M et al (2012) Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets. Nature 486(7403):420–428
International Gene Synthesis Consortium (2017) Harmonized screening protocol V2.0. Gene Sequence & Customer Screening to Promote Biosecurity, 19 November 2017
Jefferson C, Lentzos F, Marris C (2014) Synthetic biology and biosecurity: challenging the "myths". Front Public Health 2:115
Kuiken T (2016) Should we fear DIY biologists' use of cutting-edge gene-editing technology? Scientific American, 18 March 2016
Lai H et al (2019) Synthetic biology and the United Nations. Sci Soc 37(11):1146–1151. https://doi.org/10.1016/j.tibtech.2019.05.011
Ledford H (2010) Garage biotech: life Hackers. Nature 467:650–652. https://doi.org/10.1038/467650a

Lentzos F, Hamilton RA (2010) *BWC Confidence Building Measures: Preparing for a comprehensive review of the CBM mechanism at the Seventh BWC Review Conference*. London School of Economics

Linkov I, Trump BD, Anklam E, Berube D, Boisseasu P, Cummings C et al (2018a) Comparative, collaborative, and integrative risk governance for emerging technologies. Environ Syst Decis 38:170–176

Linkov I, Trump BD, Poinsatte-Jones K, Florin MV (2018b) Governance strategies for a sustainable digital world. Sustainability 10(2):440. Decisions 38(2):170–176

Marchant GE, Allenby BR, Herkerts JR (2011) The growing gap between emerging technologies and legal-ethical oversight: the pacing problem. Springer, New York

McCarty A (2018) Changes in U.S. biosecurity following the 2001 Anthrax attacks. J Bioterror Biodef 9(2). https://doi.org/10.4172/2157-2526.1000163

McLeish C, Nightingale P (2007) Biosecurity, bioterrorism and the governance of science: the increasing convergence of science and security policy. Res Policy 36:1635–1654

Mumford JD, Leach AW, Holt J, Suffert F, Sache I, Moignot B, Hamilton RA (2017) Integrating crop bioterrorism hazards into Pest risk assessment tools. In: Gullino ML, Stack JP, Fletcher J, John D (eds) Practical tools for plant and food biosecurity. Springer, Mumford

National Research Council (2004) Biotechnology research in an age of terrorism. The National Academies Press, Washington, DC. https://doi.org/10.17226/10827

National Science Advisory Board for Biosecurity (2006) Addressing biosecurity concerns related to the synthesis of Select Agents. Report of the National Science Advisory Board for Biosecurity (NSABB), December 2006

National Science Advisory Board for Biosecurity (NSABB) (2011) Strategies to educate amateur biologists and scientists in non-life science disciplines about dual use research in the life sciences. Report of the National Science Advisory Board for Biosecurity, June 2011

Ney P, Koscher K, Organick L, Ceze L, Kohno T (2017) Computer security, privacy, and {DNA} sequencing: compromising computers with synthesized {DNA}, privacy leaks, and more. In 26th {USENIX} Security Symposium ({USENIX} Security 17): 765–779

Noyce RS, Lederman S, Evans DH (2018) Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments. PLoS One 13(1):e0188453

Ossola A (2016) Why is the FBI reaching out to student bioengineers? Vice, 26 November 2016. Available: https://www.vice.com/en_us/article/yp3knm/igem-fbi. Last accessed 26 Sept 2019

Oye K (2012) Proactive and adaptive governance of emerging risks: the case of DNA synthesis and biotechnology. IRGC, Public Sector Governance of Emerging Risks, Synthetic Biology Case, June 2012

Palumbo A, Bellamy R (2010) From government to governance. Taylor & Francis LTD, New York

Pauwels et al (2013) Event report: SynBio workshop (Paris 2012) – risk assessment challenges of synthetic biology. J Verbr Lebensm 8(3):215–226

Presidential Commission for the Study of Bioethical Issues (2010) New directions. The ethics of synthetic biology and emerging technologies, December 2010

Regalado A (2016) Top U.S. intelligence official calls gene editing a WMD threat. MIT Technology Review, 9 February 2016. https://www.technologyreview.com/s/600774/top-us-intelligence-official-calls-gene-editing-a-wmd-threat/

SCENIHR, SCHER and SCCS (2015) Final opinion on synthetic biology III: risks to the environment and biodiversity related to synthetic biology and research priorities in the field of synthetic biology. European Union 2015. https://doi.org/10.2875/590512

SCHER, SCENIHR and SCCS (2014) Opinion on synthetic biology 1: definition. European Union 2014. https://doi.org/10.2772/76553

Stirling A (2006) Precaution, foresight and sustainability: reflection and reflexivity in the governance of science and technology. Reflexive Gov Sustain Dev 225

Trump BD (2017) Synthetic biology regulation and governance: lessons from TAPIC for the United States, European Union, and Singapore. Health Policy 121(11):1139–1146

Trump BD, Galaitsi SE, Appleton E, Bleijs DA, Florin MV, Gollihar JD et al (2020) Building biosecurity for synthetic biology. Mol Syst Biol 16(7):e9723

Wager R, McHughen A (2010) Zero sense in European approach to GM: the European Union's zero-tolerance of trace amounts of unapproved genetically modified material in imported food and feed is scientifically unsound and could lead to economic ruin. EMBO Rep 11(4):258–262

Weintraub K (2019) Scientists call for a moratorium on editing inherited genes. Scientific American, Policy and Ethics. https://www.scientificamerican.com/article/scientists-call-for-a-moratorium-on-editing-inherited-genes/

World Health Organization (2012) Report on technical consultation on H5N1 research issues. Geneva, 16–17 February 2012. Available at: https://www.who.int/influenza/human_animal_interface/mtg_report_h5n1.pdf. Accessed 18 Jan 2020

World Health Organization (2015) The independent advisory group on public health implications of synthetic biology technology related to smallpox. WHO/HSE/PED/2015. World Health Organization, Geneva. Available at: https://apps.who.int/iris/bitstream/handle/10665/198357/WHO_HSE_PED_2015.1_eng.pdf;jsessionid=C3EDD415EB9BDC07097AAB2FB707F1B0?sequence=1. Accessed 20 Dec 2019

ZKBS (2018) Synthetic biology. 2nd Interim report of the German Central Committee on Biological Safety, June 2018