Chapter 7
Security Issues Related to Synthetic Biology

Between Threat Perceptions and Governance Options

Alexander Kelle

Contents

Abstract Given the historical pattern of misuse of advances in the life sciences, the biosecurity implications of synthetic biology deserve close attention. This requires in the first instance a clear understanding of the differences between traditional biosafety concerns and potential biosecurity threats. After discussing the meaning attached to these terms, the paper moves on to analyse the biosecurity awareness of synthetic biologists in Europe in relation to several of the key events in the evolving biosecurity discourse. Following the analysis of interview results that reveal a low to medium level of biosecurity awareness on the part of European synthetic biologists,

A. Kelle (✉)
Department of European Studies and Modern Languages, University of Bath, Claverton Down, Bath BA2 7AY, UK; Organisation for International Dialogue and Conflict Management (IDC), Biosafety Working Group, Vienna, Austria
e-mail: a.kelle@bath.ac.uk; alexander.kelle@idialog.eu

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biosecurity governance mechanisms are evaluated that have been proposed up to now. These put either a heavy emphasis on self-governance by the synthetic biology community, or focus on technical solutions to address biosecurity risks. Expanding on these proposals the chapter outlines a new 5P-strategy for synthetic biology biosecurity governance which revolves around a set of measures being identified that could be brought to bear at the identified five policy intervention points.

7.1 Introduction

Over the past few years synthetic biology has developed into one of the most dynamic sub-fields of the life sciences (O'Malley et al. 2008, POST 2008, van Est et al. 2007). It has come to be used as the umbrella term for different approaches ranging from large-scale assembly of DNA segments to the developments of new tools and technology platforms to the search for the minimal cell and the origins of life.[1]

Coupled with the development of the field so far was the recognition of the potential societal implications and dangers that might emanate from the shift in biology from a descriptive to a predictive science in which the functions of genetic code are well understood and allows for the "programming" of not only beneficial but also malicious biological code.

Treating these dangers seriously (Selgelid 2007) appears warranted because of at least two sets of reasons, the first of which is related to a pattern of past misuse of advances in the life sciences. As Dando (1999) has outlined for the twentieth century, major scientific breakthroughs have repeatedly been exploited by offensive state-level biological weapons (BW) programmes. This applies to bacteriology at the back end of the nineteenth century through to aerobiology and virology in the middle of the twentieth century and to the early stages of genetic engineering, the latter of which found its way into the clandestine Soviet BW programme of the 1970s and 1980s. This pattern of past utilization of the latest scientific advances for BW developments raises the spectre of twenty-first century advances in the life sciences also being redirected into state-level efforts to produce novel BW or to simplify the acquisition of known biological warfare agents.

One recent study on the impact of biotechnology more generally on biological warfare and biodefense (Petro et al. 2003) has pointed to the second set of reasons for a potential interest in designing advanced biological warfare agents that bear little to no resemblance to traditional BW: advances in biodefense measures against traditional BW and the finite number of suitable candidate pathogens and toxins for BW purposes. In light of these two limitations for offensive biological warfare, such advanced biological warfare agents may provide the capability to overwhelm even the most robust defences. In the words of Petro and colleagues:

[1] For a more detailed discussion of the different strands of synthetic biology see Chapter 3 by Lam C, Godinho M, dos Santos V (2009) in this volume.

> Unlike threats posed by traditional and genetically modified traditional agents, the capability-based threat posed by ABW [advanced biological warfare, AK] agents will continue to *expand indefinitely* in parallel with advances in biotechnology. (Petro et al. 162, emphasis added)

It should not come as a surprise that different sub-strands of synthetic biology[2] have different kinds of security implications that already are or will become relevant at different points on a temporal continuum. Clearly, the potential security implications of synthetic genomics with its large-scale quick turn-around mail-order DNA synthesis capacities are of a much more immediate concern than those of some future cell with a minimal genome that can serve as the chassis for applications even further down the line.

The following analysis of security issues related to synthetic biology will start with a discussion of different terms that have been utilized in this context, most notably risk, biosafety and biosecurity. The subsequent part of the chapter will then present in abbreviated form the findings of a set of 20 interviews with European synthetic biology practitioners that were conducted in summer and fall of 2007, primarily during the SB3.0 conference in Zurich. Following from this, the penultimate section will outline some proposals to start a debate on possible future biosecurity governance options for synthetic biology. The final part of the chapter will summarize the argument and offer some concluding thoughts.

7.2 Risks, Safety and Security: Coming to Terms with Terminology

The potential risks inherent in this new powerful technology have been a recurrent topic amongst synthetic biology practitioners, commentators and national and international institutions alike (Balmer and Martin 2008, Bhutkar 2005, Carlson 2003). A 2005 NEST High-Level Expert Group study commissioned by the European Commission for example acknowledged that

> genetic manipulation of organisms can be used or can result by chance in potentially dangerous modifications of human health or the environment. The possibility of designing a new virus or bacterium à la carte could be used by bioterrorists to create new resistant pathogenic strains or organisms, perhaps even engineered to attack genetically specific sub-populations. (European Commission 2005)

As the chairman of the NEST High-Level Expert Group in a more recent study reaffirmed (Serrano 2007),

> The main concern in Biosecurity arises however from the possibility that rogue states or terrorists organization re-engineered microorganisms, or living systems with the purpose to harm. Although this seems scary, it is not yet so simple to create a new pathogenic organism and to release it in an effective way.

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[2] See in Chapter 3 by Lam et al. 2009, Chapter 6 by Schmidt 2009, both in this volume

However, Serrano cautions that existing "hurdles and the engineering challenges they currently represent may ... be overcome in some near future by further advances in science and we need thus to keep vigilant" (2007: 2). This assessment is shared by Garfinkel et al. (2007) who conclude that "in the near future ... the risk of nefarious use will rise because of the increasing speed and capacity" (Ibid: 12) of synthetic genomics, one of the key enabling technologies identified in the report of the NEST High-Level Expert Group (2005).

Along similar lines Tucker and Zilinskas (2006) also distinguish between possible misuse by both state and sub-state actors. More generally, they identify three categories of risk flowing from synthetic biology:

> First, synthetic microorganisms might escape from a research laboratory or containment facility, proliferate out of control, and cause environmental damage or threaten public health. Second, a synthetic microorganism developed for some applied purpose might cause harmful side effects after being deliberately released into the open environment. Third, outlaw states, terrorist organizations, or individuals might exploit synthetic biology for hostile or malicious purposes. (Ibid: 31)

In the third threat scenario they point out two categories of actors of potential concern: the "lone operator" and "the biohacker". While the lone operator is a rogue synthetic biologist – comparable to the Fort Detrick researcher who is now believed to be responsible for posting the 2001 anthrax letter attacks in the USA – the ideal type bio-hacker is a college student eager to demonstrate their technological prowess. In this they may accidentally create a security problem or be guided by malicious intent. This clearly shows that the issue of do-it-yourself biology or a bio-hacker culture developing is not only a biosafety issue, but needs to be monitored from a biosecurity perspective as well.

The diverse nature of potential risks associated with synthetic biology has also informed a recent study by the International Risk Governance Council (IRGC 2008). The authors of the IRGC study identify what they call "environmental risks" (biosafety) and "social risks" (biosecurity) and rightly point out that discussion of the latter has been more prevalent in the US academic and political discourse than in Europe or elsewhere (Choffnes, Lemon and Relman 2006).

The distinction between biosafety and biosecurity has been a point of discussion also outside the synthetic biology context, e.g. in the framework of the annual meetings of the states parties to the Biological and Toxin Weapons Convention (BWC). Usually, usage of the terms biosafety and biosecurity draws on the WHO guidelines on laboratory biosafety and laboratory biosecurity (WHO 2004, 2006, Schmidt 2008). However, as a background document prepared by the Implementation Support Unit of the BWC states parties for an expert meeting in August 2008 stated

> Biosafety is a well-established concept with a widely-accepted meaning and international guidance on how it is put into practice at the national level. Biosecurity is a comparatively new term, with divergent meanings depending upon the setting in which it is used.

The ISU background document further quotes one unnamed diplomat as having offered the bon mot that *Biosafety protects people from germs – biosecurity protects germs from people* (Ibid: 3). Pursuing biosafety and biosecurity goals are

thus mostly complementary activities with a large area of overlap between them. However, in certain instances approaches to achieve biosecurity and biosafety may be at odds.

An example of biosafety measures not necessarily supporting biosecurity goals is found in the notion of engineering biosafety mechanisms into synthetic organisms, so that they for example depend on nutrients that they cannot find in nature. Yet, the principal problem with such an approach is that if such a safety system has to be engineered into a synthetic organism, someone with malicious intent could possibly engineer such a fail-safe mechanism out of the organism. Thus some biosafety strategies may go some way in addressing biosecurity concerns, but there certainly is not a complete overlap. Biosecurity issues thus need to be addressed in their own right.

7.3 Biosecurity Awareness of Synthetic Biology Practitioners in Europe

Some of the governance approaches that have been proposed for synthetic biology[3] rely on some form of involvement of the scientific community in these activities (Maurer and Zoloth 2007). One of the key pre-requisites of any degree of involvement is, of course, a certain level of awareness of the relevant issues on part of the synthetic biology community. This applies in particular to the realm of biosecurity, as there is no prior engagement of the scientific community to the extent that other ethical, social, and legal issues (ELSI) have been discussed in for example past debates on genetically modified organisms (de Vriend 2006). In order to assess the level of awareness of the unfolding biosecurity discourse, 20 leading European SB practitioners have been interviewed between June and October 2007. These interviews set out to investigate the awareness of European synthetic biologists of dual-use issues and proposals in relation to the key manifestations of an increasingly active discourse on security implications of the life sciences. These six studies or institutional activities were selected for their importance in advancing the debate and understanding of the dual-use risks inherent in the revolution in the life sciences with respect to synthetic biology or for the proposed solutions to the identified biosecurity issues. In short, they have been the key markers in the developing biosecurity discourse.

7.3.1 The Fink Committee and Its Recommendations

The work of the Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology, the so-called the Fink Committee, was a reaction to increasing concerns in the US that research in the life sciences might be

[3] This section draws heavily on the author's report *Synthetic Biology and Biosecurity Awareness in Europe* (Kelle 2007)

misused for bioterrorist or biowarfare purposes (National Research Council 2004). These concerns, in turn were fuelled by a number of experiments that triggered substantial debate about the advisability of such research, whether it should be carried out, or, if carried out, its results should be published.

Against this background the Committee was specifically tasked to "recommend changes in... practices that could improve U.S. capacity to prevent the destructive application of biotechnology research while still enabling legitimate research to be conducted." (National Research Council 2004: 32) Although the NRC is not a government body that can promulgate laws or regulations, its recommendations are often put into practice by the United States government and also have an agenda-setting function in scientific and academic discourse. In the case of the Fink Committee's seven recommendations this pattern has repeated itself. The recommendations are:

- Educating the Scientific Community.
- Reviewing Plans for Experiments.
- Reviewing at the Publication Stage.
- Creation of a National Science Advisory Board for Biodefense.
- Adoption of Additional Elements for Protection Against Misuse.
- A Role for the Life Sciences in Efforts to Prevent Bioterrorism and Biowarfare
- Harmonized International Oversight.

Of the 20 interviewees only seven had heard of the report and only one interviewee provided an opinion on its above mentioned recommendations: according to this interviewee the Fink Committee's recommendations are sensible and show the difficulty inherent in any attempt to suggest oversight or governance measures for synthetic biology, i.e., that of having to walk a tightrope between measures that are effective enough to prevent misuse and at the same time are not too restrictive so as to limit scientific and technological progress.

7.3.2 The Lemon Relman Committee Report

Shortly after the Fink Committee report was published, the US NAS set up the Committee on Advances in Technology and the Prevention of their Application to Next Generation Bioterrorism and Biological Warfare Threats, the so-called Lemon-Relman Committee, named after its two co-chairmen. This Committee expanded on the work of the Fink Committee in several directions (National Research Council 2006): first, its focus was global, not confined to the US; second, it adopted a forward-looking approach, trying to distil scientific and technological trends that would impact on the biothreat spectrum over the next 5 to 10 years, and; third, it rejected the limitation of its work to traditional biowarfare agents as too narrow.

A concise discussion of the future applications of synthetic biology in the report acknowledges that "DNA synthesis technology could allow for the efficient, rapid synthesis of viral and other pathogen genomes – either for the purposes of vaccine or therapeutic research and development, or for malevolent purposes or with unintended consequences." (Ibid: 109)

It is thus fair to conclude that the Lemon-Relman Committee had clearly identified synthetic biology as one of the technologies that will have a major impact on the future biothreat spectrum. In line with this reasoning the Committee recommended to

> adopt a broadened awareness of threats beyond the classical "select agents" and other pathogenic organisms and toxins, so as to include, for example, approaches for disrupting host homeostatic and defense systems, and for creating synthetic organisms. (Ibid: 177f)

In marked contrast to the increasingly careful monitoring and analysis of developments in synthetic biology by biosecurity experts, none of the interviewed synthetic biology practitioners had heard of the Lemon-Relman Committee, its report or any of the report's recommendations.

7.3.3 Draft Declaration of the Second International Meeting on Synthetic Biology

As the draft Declaration of the Second International Meeting on Synthetic Biology (SB2.0) demonstrates, societal implications are taken seriously by many in the SB community. In case of the SB 2.0 a full day was devoted to discussion of such issues and the subsequently formulated declaration of May 2006 contains four resolutions that clearly aim at addressing some of the dual-use implications of synthetic biology, in particular DNA synthesis that may give rise to safety or security concerns. (Conferees, SB2.0 2006) The focus on DNA synthesis is also reflected in two of the four resolutions contained in the final declaration. In terms of practical next steps to be pursued, the draft declaration proposes the formation of an open working group in support of the improvement of existing software tools for screening DNA sequences, as well as the completion of a study to develop governance options for DNA synthesis technology.

When asked about their awareness of the draft declaration of SB 2.0 and its contents, more than half of the interviewees, 12 out of 20, said they were aware of the declaration. This is a markedly higher level of awareness when compared to the previous two studies that were external to the synthetic biology community's own attempts to address biosecurity concerns. However, of the 12 positive respondents only three were in a position to give an assessment of the four resolutions contained in the SB 2.0 declaration.

7.3.4 CSIS-MIT-Venter Report on the Governance of Synthetic Genomics

Half of all interviewees were aware of the CSIS-MIT-Venter (draft) report on Synthetic Genomics (Garfinkel et al. 2007), to which the SB 2.0 declaration had made explicit reference.

Because some of the interviews were conducted during or after SB 3.0 when the draft report was presented in the panel session on societal issues, these results are likely to have been affected by the timing of the interviews in relation to the presentation. Support for this assumption can be derived from the fact that two interviewees made explicit reference to the presentation when answering the question. It is also noteworthy that only two of the respondents who had knowledge of the draft report were able to provide an assessment of the policy options put forward in the report.

Considering the study's assumptions and the character of the policy options it is presenting, it is noteworthy that

> today, any synthesis of viruses, . . . remains relatively difficult. In the near future, however, the risk of nefarious use will rise because of the increasing speed and capability of the technology and its widening accessibility. (Ibid: 12)

It would therefore appear that there is a window of opportunity available *now* to devise and implement the most effective governance system to prevent the misuse of synthetic biology in the future. Given this urgency, it is somewhat puzzling that the authors of the report stress at several points that they are only providing policy options, and are not making recommendations. On a different level it is also questionable whether this self-selected detachment is actually sustainable: clearly, through presenting and discussing some options, but not others, the issues are framed in a certain way that cannot but influence discussions in the policy-making process. For doing this in a particular way, the report was immediately criticized from two different groups: while according to the *ETC Group* the report represented only a "partial consideration of governance by a partisan group of authors" which "overlooks important questions related to power, control and economic impacts of synthetic biology" (ETC Group 2007), the *Sunshine Project*– which has been a long-standing critic of the performance of IBCs – focused on the expanded role foreseen in the report for Institutional Biosafety Committees (IBC) in overseeing synthetic biology (www.sunshineproject.org).

7.3.5 The Work of the NSABB and Its Synthetic Biology Working Group

Following one of the recommendations contained in the Fink Committee Report, the US government set up the National Science Advisory Board for Biosecurity (NSABB) in March 2004. The Board's activities range from developing "criteria for identifying dual-use research and research results" to "guidelines for the oversight

of dual-use research, including guidelines for the risk/benefit analysis of dual-use biological research and research results" to the recommendation of "strategies for coordinated international oversight of dual-use biological research." One of the working groups that the NSABB has created to address more specific issues has focused its attention on the new field of synthetic biology. In the first phase of its work, the NSABB synthetic biology working group sought to address biosecurity implications of the de novo synthesis of select agents. A preliminary report of the synthetic biology working group was discussed during a NSABB meeting in October 2006 and has subsequently been submitted to the US government and made available to the public. (NSABB 2006) The report recommends to the US government inter alia that

> ... HHS and USDA collaboratively develop and disseminate harmonized guidance to investigators and nucleic acid/gene/genome providers concerning the SAR with respect to synthetically-derived DNA ...
>
> ... relevant federal agencies ... develop a process to be used by providers of synthetic DNA for determining the sequences for which to screen (Select Agents or otherwise) ...
>
> ... convene a group of experts from the scientific community to conduct an open and in depth examination of the Select Agent classification system to determine if it is possible to reconcile the current controls for Select Agents with the anticipated scientific advances enabled by synthetic genomics ... (Ibid: 10–13)

Less than one fifth of interviewees (3 out of 20) were aware of the NSABB activities and its synthetic biology working group report. Of those who had heard of the report, none was in a position to offer an assessment as to its content or recommendations.

7.3.6 The Controlling Dangerous Pathogens Project at the University of Maryland

Since 2002 a group of scholars at the University of Maryland, led by John Steinbruner, has developed a protective oversight system for dangerous biological agents and research. (Steinbruner 2002) The most elaborate version of this proposal has been published as a monograph in spring 2007. (Steinbruner et al. 2007) Starting from the dual-use dilemma inherent in most, if not all of life sciences research, Steinbruner and colleagues argue the case for "an oversight process designed to bring independent scrutiny to bear throughout the world without exception on fundamental research activities that might plausibly generate massively destructive or otherwise highly dangerous consequences." This proposal goes far beyond any of the other recommendations considered so far in two ways: first of all, it advocates subjecting all, not just publicly funded, research to independent scrutiny, and second, the proposal's scope is global, not just national. Steinbruner and colleagues argue further that

> inherently dangerous areas of biological research will have to be subjected to a much more systematic process of protective oversight than is yet practiced in any country. That will have to be done globally and therefore will have to be globally formulated and globally implemented. (Ibid: 6)

Such research is then broken down into three categories of activities, each of which will necessitate different levels of scrutiny: activities of potential concern will be subjected to local peer review oversight, activities of moderate concern to national oversight and activities of extreme concern will receive the highest level of scrutiny on the international level. In order for the peer review process to work at each of the three levels, a wide-ranging licensing of relevant individuals and research facilities will be required.

When asked about their awareness of the existence of the *Controlling Dangerous Pathogens Project* conducted at the University of Maryland 6 of the 20 interviewees responded positively. As with the previous reports, the level of detailed knowledge about the "Biological Research Security Oversight System" proposed by the University of Maryland group turned out to be low: only one interviewee felt in a position to provide an assessment of the group's work.

7.3.7 Summary of Interview Results

In sum, this set of 20 interviews has brought to the fore a low to medium level of awareness in *quantitative* terms on part of European synthetic biology practitioners in relation to key developments and reports in the biosecurity area. Around a third of interviewees had heard of the Fink Committee and its report, and none was aware of the Lemon-Relman Committee and its call to broaden our understanding of the biosecurity threat to include synthetic organisms. The only landmark in the emerging biosecurity discourse among synthetic biologists to receive a level of awareness of more than 50% is the SB 2.0 declaration discussed above, with the CSIS-MIT-Venter report receiving the second highest awareness score. Awareness of NSABB activities with respect to synthetic biology or the University of Maryland *Controlling Dangerous Pathogens Project* are below the 50% mark, in case of the NSABB the level of awareness is even down to 15%.

In *qualitative* terms the picture is even bleaker: only a small part of interviewees, if any at all, were in a position to give an assessment of the various Committees, reports and recommendations addressed in the interview. Even in the case of the SB 2.0 declaration the level of awareness dropped from 60 to 15%, when considering this qualitative dimension. This somewhat superficial knowledge on part of many who were in principle aware of the unfolding biosecurity discourse with respect to the life sciences in general and synthetic biology in particular poses another obstacle to a constructive participation by synthetic biology practitioners in that very discourse (see Table 7.1.).

Clearly, debates have moved on somewhat since the conduct of these interviews in the second half of 2007. The extent to which this has led to an increased awareness is unclear, but as no concerted effort at biosecurity awareness-raising or education of synthetic biologists has been undertaken, any increase in the level of awareness is very likely to be of an incremental nature.

Table 7.1 Awareness of the developing biosecurity discourse among European synthetic biology practitioners

Question no.	Yes	No
1. Fink committee	7	13
2. Lemon-Relman committee	0	20
3. SB 2.0 declaration	12	8
4. CSIS-MIT-Venter report	10	10
5. NSABB synthetic biology WG	3	17
6. Controlling dangerous pathogens project	6	14

7.4 Biosecurity Governance Options for Synthetic Biology

In light of the level of biosecurity awareness among synthetic biologists (especially in Europe), any governance system will have to include measures to raise such awareness in the scientific community. Over the course of the past few years some proposals for such governance systems or parts thereof have been proposed by different scholars and institutions. These will be briefly discussed in the following section.

7.4.1 Proposals for Biosecurity Governance

One of the earliest proposals for the oversight of synthetic biology was put forward by George Church with his "Synthetic Biohazard Non-proliferation Proposal" (Church 2004). In it he suggests to screen DNA and oligonucleotide orders for similarity to select agents, as well as to license certain instruments and reagents, so as to limit their proliferation. Both of these suggestions have subsequently been taken up in initiatives and proposals by other groups or institutions (see below). With respect to oversight and regulation of these obligations, Church considers the option of setting up a clearinghouse with oversight assigned to one or more US federal agencies, like the Center for Disease Control, the Department of Homeland Security or the FBI.

In contrast, a White Paper that was circulated in the run up to the SB2.0 conference by Maurer et al. (2006) put a greater emphasis on options that "can be implemented through community self-governance without outside intervention."(Ibid: 2) The document contained several recommendations for such community action which were fed into the deliberations during SB2.0 and almost resulted in a consensus document being adopted by conference participants, had it not been for the massive criticism of a group of 35 civil society organisations (ETC Group 2006). Thus, there is just a draft declaration available on the internet, which, however, was never formally adopted.

As mentioned above (see Section 7.3.3) one of the resolutions of the draft SB2.0 declaration made reference to a study on governance options for synthetic genomics which eventually was published in late 2007 (Garfinkel et al. 2007). The report "Synthetic Genomics: Options for Governance" does not only address biosecurity issues stemming from the broad array of new capabilities provided by synthetic genomics, but does also address environmental and biosafety risks. The most effective intervention point for preventing the misuse of synthetic genomics identified by the authors of the report is at the level of DNA synthesis itself, i.e., gene synthesis firms, oligonucleotide manufacturers and DNA synthesizers. Thus, policy options discussed were from a biosecurity point of view assessed in terms of their usefulness in preventing incidents of bioterrorism or by helping to respond to such incidents after they had occurred. For both gene foundries and oligo manufacturers the authors of the report concluded that a combination of screening orders by companies and the certification of orders by a biosafety/biosecurity officer provide the greatest benefits in terms of preventing incidents. For helping to respond after an incident had occurred, the storage of order information by firms was regarded as the most useful tool. Finally, with a view to equipment such as DNA synthesizers, the report concluded that the licensing both of equipment and of reagents was most useful to enhance biosecurity by contributing to the prevention of incidents of misuse.

This study on the governance of synthetic genomics in turn has clearly influenced the work of two further groups, which also shows a clear trend of the increasing involvement of DNA synthesis companies and their industry associations in the formulation of responses to potential biosecurity threats emanating from synthetic biology and its applications. This is a positive and noteworthy development.

The first of these groups, the International Consortium for Polynucleotide Synthesis (ICPS) has put forward a "tiered DNA synthesis order screening process." (Bügl et al. 2007) According to this proposal

> individuals who place orders for DNA synthesis would be required to identify themselves, their home organisation and all relevant biosafety [sic] information. Next, individual companies would use validated software tools to check synthesis orders against a set of select agents or sequences to help ensure regulatory compliance and flag synthesis orders for further review. Finally DNA synthesis and synthetic biology companies would work together through the ICPS, and interface with appropriate government agencies (worldwide), to rapidly and continually improve the underlying technologies used to screen orders and identify potentially dangerous sequences, as well as develop a clearly defined process to report behavior that falls outside of agreed-upon guidelines. (Ibid: 627)

This proposal would put DNA synthesis companies and their industry association at the centre of a governance structure that would, however, not be a self-contained system of oversight, but rather rely on "agreed-upon guidelines". Such guidelines would be operationalized inter alia through lists of "select agents or sequences" that would determine whether and how to process DNA synthesis orders on the part of those companies that follow the guidelines.

Efforts of the second industry association in the area of synthetic biology, the Industry Association Synthetic Biology (IASB) have recently focussed on a number of different, but interrelated issues. These were formulated and moved forward during a workshop that was held in Munich in April 2008 on "Technical

solutions for biosecurity in synthetic biology" (IASB 2008). Motivated by "our responsibility for the scientific field to which we provide services and products" (Ibid: 2), workshop participants – which included also members of ICPS and independent academics – agreed on the adoption of five distinct work packages:

1. Harmonization of screening strategies for DNA synthesis orders;
2. Creation of a central virulence factor database;
3. Publication of an article on the status quo of synthetic biology;
4. Establishment of a technical biosecurity working group with members from both organisations in order to "discuss improvements and next steps for biosecurity measures", and;
5. Formulation of a code of conduct. (Ibid: 16 f.)

Obviously both these work packages and future efforts by IASB and ICPS will have the greatest impact when implemented by as many companies as possible in the field of DNA synthesis. To achieve this end, the fifth work package is of particular relevance. The drafting of such a code was suggested during the April 2008 workshop and an initial text was presented at the 2008 BWC meeting of states parties in Geneva in December. This code seeks to establish high-standard biosecurity DNA synthesis screening as industry best practice, will commit its signatories to keep records of suspicious inquiries and positive screening hits as well as to inform authorities about such orders and inquiries that indicate illegal procurement activities (IASB 2008).

In sum, two trends are discernible in current proposals for biosecurity governance of synthetic biology. The first of these is one driven by DNA synthesis companies and their industry associations who place the focus of their activities on technical solutions to the problem of potential misuse of the DNA sequences they provide. Here the emphasis is on the formulation and implementation of best practices across the industry. Oversight and enforcement of these standards, however is not regarded as falling into the purview of industry itself. As clearly spelled out in the IASB workshop report, "[u]ltimately, the definition of standards and the enforcement of compliance with these is a government task" (2008: 14). The second – not easily reconcilable – trend seems to be driven by those in the synthetic biology community who are advocating self-governance by the scientific community as the prime or even sole approach to follow. Somewhat puzzling in this context is the assertion by some that "initiatives developed by the synthetic biology community may be more effective than government regulation precisely because they are more likely to be respected and taken seriously" (Maurer and Zoloth 2007) Clearly, DNA synthesis companies, who are currently at the forefront of formulating proposals and thus setting the agenda as far as technical solutions are concerned, are not adverse to government oversight and regulation. As one of the industry contributors to the SYNBIOSAFE e-conference in spring 2008 pointed out, such oversight and regulation have two distinct advantages (Schmidt et al. 2008). It firstly will "reassure the public that biosafety and biosecurity concerns are addressed" and it secondly "would provide legal security to the industry, by defining clear compliance rules" (SYNBIOSAFE 2008: 45). The

above assertion about the greater likelihood of self-governance measures being observed also seems to fly in the face of evidence of select agent rules being followed by the scientific community in the US and more general regulation on genetically modified organisms being observed by researchers and industry alike.

7.4.2 The 5P-strategy for Synthetic Biology Biosecurity Governance

While the proposals for technical solutions to biosecurity of DNA synthesis certainly are to be welcomed and provide useful building blocks for a overarching synthetic biology biosecurity governance structure, they do not represent an integrated approach that would, for a start, also include a coherent set of awareness raising measures across the synthetic biology community. Furthermore, due to the mostly technical character of the solutions proposed and their focus on currently existing problems in a sub-field of synthetic biology these initiatives are not likely to be applicable to the full spectrum of synthetic biology approaches, many of which at the moment are still at the proof of principle stage.

What is thus needed is a broader-based approach that (a) includes all stakeholders in the development of synthetic biology as a discipline and its potential future applications, and (b) is flexible enough to accommodate a range of scenarios of how the field might develop. To facilitate the development of such an overarching governance structure a 5P-strategy is proposed that focuses its attention on five different policy intervention points: the

- principal investigator (PI), the
- project, the
- premises, the
- provider (of genetic material) and, its
- purchaser.

This would expand for example the suggested policy intervention points considered by the study on synthetic genomics mentioned above (Garfinkel et al. 2007), which placed the emphasis on DNA synthesis companies (providers) and its customers. Although one can argue that the screening of customers provides some biosecurity benefits, it does not apply the full spectrum of potentially available measures to minimise biosecurity concerns.

At each of the five policy intervention points, a number of different measures are conceivable in order to address biosecurity concerns, depending on their severity. Again, quite a few of these are potential threats whose precise manifestation is not clear yet, so that at this point in time no definite threat assessments can be conducted and consequently the appropriate level of response cannot be known. In principle, the biosecurity measures for synthetic biology range from awareness raising on part

Table 7.2 Potential biosecurity measures in the context of the 5P-strategy

Potential biosecurity measures	Policy intervention points				
	Principal investigator	Project	Premises	Provider	Purchaser
Awareness raising					
Education/training					
Guidelines				X	
Codes of conduct				X	
Regulation				X	
Natl. laws	(X)	(X)	(X)	X	(X)
International treaty/agreement	(X)	(X)	(X)	X	(X)

of the involved synthetic biologists to education and training, codes of conduct, regulation, national laws, and international treaties.

The prime international legal instrument to prevent the use of biology for weapons purposes is the 1972 BWC. While in principle also covering developments in the field of synthetic biology, there are two fundamental problems associated with the BWC having concrete biosecurity benefits in practical terms: first, provisions of the BWC are so general that they do not provide specific guidance. For this the more concrete rules and procedures written into national implementing legislation are required. Unfortunately, many state parties to the BWC have enacted only insufficient national legislation implementing the BWC or none at all. The second problem lies in the absence of any verification provisions in the BWC – there is thus no way to inspect facilities in states parties on a regular basis, so as to verify that no activities that are prohibited under the treaty are taking place. As the scope of the BWC and existing implementing legislation in states parties might also not cover all synthetic biology facilities or activities the corresponding fields in the following table have been marked in parentheses only (see Table 7.2.).

As should be obvious from the previous discussion, the fields marked without such parentheses all relate to activities conducted by DNA synthesis companies or their industry associations. On an international level the screening of DNA orders that is being conducted is partially driven by the harmonised export controls by states that are participating in the so-called Australia Group. “The Australia Group (AG) is an informal forum of countries which, through the harmonisation of export controls, seeks to ensure that exports do not contribute to the development of chemical or biological weapons.” (Australia Group 2007) As part of its activities the AG maintains Common Control Lists that inter alia require controls on the export of certain biological agents or parts thereof. More specifically the control list covers

1. Genetic elements that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the list.
2. Genetic elements that contain nucleic acid sequences coding for any of the toxins in the list, or for their sub-units.

3. Genetically-modified organisms that contain nucleic acid sequences associated with the pathogenicity of any of the microorganisms in the list.
4. Genetically-modified organisms that contain nucleic acid sequences coding for any of the toxins in the list or for their sub-units. (Australia Group 2006)

These lists are being implemented through national laws and regulations, but clearly require states participating in the AG only to regulate exports of such material, not domestic transfers. As the IASB report has pointed out "legislation for domestic orders is much more relaxed – both in the USA and the EU. Such legislation is much more focussed on biosafety than biosecurity". (IASB 2008: 7) Thus, the additional biosecurity screening of domestic orders and customers by DNA synthesis companies is de facto done on a voluntary basis, following company guidelines. The harmonisation of such guidelines is currently pursued through the formulation of a code of conduct by IASB for the whole industry. While it can be expected that the promotion of such a code of conduct will entail some awareness raising and education efforts in relation to those parts of the industry that do not currently screen orders, keep records, etc., no systematic efforts are under way at raising biosecurity awareness among synthetic biologists.

What is needed in addition to such efforts at awareness raising and education is a systematic analysis of which of the empty fields in the above table actually could be populated with adequate measures at the different policy intervention points. Thus, this table is not intended to suggest that all these boxes need to be ticked – rather it can serve as a tool to analyse which ones should be populated. It is more than just a remote possibility that different sub-strands of synthetic biology will require a different set of policy measures at the identified policy intervention points. On the basis of determining the range of adequate policy measures for the different branches of synthetic biology a discussion of the content of such measures can be conducted.

7.5 Summary and Conclusions

Based on the realisation that past breakthroughs in the life sciences have regularly been misused for weapons purposes, this chapter has argued that the security implications of synthetic biology need to be taken seriously. For this to be done, it is first of all necessary not to confuse or conflate the concepts of biosafety and biosecurity. While the former deals with the inherent risk of a biological agent or material to cause unintentional harm to human health or the environment, the latter is concerned with either the misuse of a biological agent or material – through for example loss, theft, diversion or intentional release – or through inadvertent research results that have security implications.

A basic pre-requisite for the formulation of meaningful and practicable biosecurity measures is the involvement of all stakeholders, including first and foremost the synthetic biology community. However, for this community to make a constructive contribution to the evolving discourse, a sufficiently well developed level of

biosecurity awareness is necessary. It was in exactly this area that a study conducted in the SYNBIOSAFE context revealed a number of gaps on the part of synthetic biology practitioners in relation to their awareness of the unfolding biosecurity discourse. While some of these gaps will have been closed through the continued exposure of synthetic biologists to the notion that biosecurity considerations do form part of their responsibilities as practicing life scientists at conferences such as the SBx.0 conference series, such exposure is likely to have led to an incremental increase, not a huge leap forward in terms of biosecurity awareness.

A review of currently existing proposals for the biosecurity governance of synthetic biology brought to the fore two main lines of reasoning and activities: one that puts a heavy emphasis on self-governance by the synthetic biology community to prevent misuse, and another one that emphasises technical solutions to address biosecurity risks. While the latter one is a necessary component of any governance or oversight system, it is by no means a sufficient to comprehensively address the full range of biosecurity issues. This is a limitation inherent in any so-called supply-side mechanisms that seek to restrict access to certain materials, technologies or know-how on the basis of list-based controls, regardless of who is implementing such measures. Attempts to formulate a code of conduct are therefore as useful and necessary a complement as comprehensive awareness raising and educational activities would be to the more technically orientated supply-side control measures that DNA synthesis companies and their industry associations are currently focussing on.

Current efforts to address biosecurity risks related to synthetic biology need to be further broadened so as to include the different strands of the scientific field to which DNA synthesis contributes. To facilitate this, a 5P-strategy has been proposed that would not only focus on the provider and purchaser of synthesised DNA, but also the principal investigator, the project, and the premises at which research is being conducted would be integrated into a comprehensive biosecurity governance system. Once the ideal policy intervention points and the measures with which to address them are determined, a discussion involving the relevant stakeholders about the content of the measures to be adopted can commence.

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