A Decade of Synthetic Biology in the Context of the Biological and Toxin Weapon Convention and the Chemical Weapon Convention

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EXECUTIVE SUMMARY

In recent years, synthetic biology has become symbolic of many of the challenges that advances in science and technology raise for the global regime prohibiting biological and chemical weapons. This has led to numerous technical reviews and governance initiatives directed at the field. However, there has been much less discussion about how experiences gained through these initiatives can help us understand existing capacities within the prohibition regime to respond to fundamental trends in innovation. Such reflection is important, as it allows us to question, in accessible and practical terms, how existing review processes might be better conceptualised and improved.

Within this paper we provide an introduction to synthetic biology as a techno-scientific field. This is followed by an introduction to a number of anticipatory security relevant initiatives which have been directed at this field. We then examine the way in which these developments have been addressed as part of international level review processes within the Chemical Weapons Convention (CWC) and Biological and Toxins Weapon Convention (BTWC).

We find that existing discussions of synthetic biology in the context of the BTWC and CWC not only point to opportunities and challenges associated with the field of synthetic biology, but also the need to develop shared principles of good practice in the areas of technology assessment and horizon scanning at both the national and international level.

This leads us to make the following recommendations:

> *Recommendation 1: It is uncertain which process States Parties will decide upon for reviewing advances in S&T at the next BTWC review conference. However, it is apparent that there is a need for states to support processes which examine the security implications of fundamental trends which the field of synthetic biology has come to symbolise. This includes, but is not limited to: automation, digitization, de-skilling and rapid commercialisation. It is essential that such processes are linked to action; in terms of norm and capacity building as well as decision making.*
>
> *Recommendation 2: In addition to reviewing the most recent scientific, technological and industrial developments in the context of the BTWC and CWC, there is a need to explore the value of the international community working together to consider, develop, and share information on approaches to technology horizon scanning and assessment as well as anticipatory governance. Such discussions could draw upon a wide range of institutional experiences in reviewing existing and foreseen security*

concerns associated with cutting-edge fields of innovation at local, national and international level. A good first step would be the convening of an international meeting which focused on these issues and brought together relevant practitioners, national level policy shapers and other stakeholders. Goals of such a meeting could include the identification and comparison of national styles of governance, as well as the identification of basic principles of good governance at local, national and international level. The field of synthetic biology may provide an accessible case study in this regard.

INTRODUCTION

With a view towards the Eighth Review Conference of the Biological and Toxin Weapons Convention (BTWC), this paper reflects on what can be learned from a decade of discussions about the field of synthetic biology. Synthetic biology gained salience at a time in which both the BTWC and the Chemical Weapons Convention (CWC) have each, in different ways, been faced with transitions. Within the BTWC regime, there has been transformation in terms of practices and priorities since the late 1990's. This has primarily resulted in a de-emphasis on formal treaty negotiations in the area of verification and an increased emphasis on the development of shared understandings and multilateral co-operation; particularly in the areas of national implementation, international cooperation as well as disease detection, surveillance and response. The Organization for the Prohibition of Chemical Weapons (OPCW) has also been faced with its own transitions as it begins to look towards a post-destruction future.

At the same time, these developments sit within a much broader context, where transformations are occurring within both domestic and international security environments as well as scientific and technological sectors.[1] Such transformations potentially affect not only the scope of issues being addressed, but also the political processes through which challenges are identified and responded to.

Within this paper we provide an introduction to synthetic biology as a techno-scientific field. This involves discussion of the key trends in this area. This is followed by an introduction to a number of anticipatory security initiatives which have been directed at this field. We then examine the way in which these developments have been addressed as part of international level review processes within the CWC and BTWC. Throughout this piece, we focus in particular on attempts to anticipate and pre-emptively engage with concerns emanating from new and emerging science and technology. We understand this to include a range of governance practices, including in the broadest sense:

- *Horizon Scanning*. Which involves systematic attempts to identify future concerns and opportunities in relation to a given area of techno-scientific innovation.

- *Technology Assessment*. Which involves the facilitation of public and political opinion formulation in relation to a given area of techno-scientific innovation. Such work helps

1 Alexander Kelle, Malcolm R Dando, and Kathryn Nixdorff, 'S&T in the Third BTWC Inter-Sessional Process: Conceptual Considerations and the 2012 ISP Meetings.' (University of Bradford: Bradford Disarmament Research Unit, 2013), http://www.brad.ac.uk/acad/sbtwc/ST_Reports/ST_Reports.htm; Mohamed Daoudi et al., 'The Future of the Chemical Weapons Convention: Policy and Planning Aspects', SIPRI Policy Paper (Stockholm International Peace Research Institute, 2013), books.sipri.org/files/PP/SIPRIPP35.pdf.

map out the specific ways in which a given technology might be incorporated into existing governance systems, or in some cases, call for adaption in those systems

Taken together then, this includes the governance practices through which institutions seek to predict advances in science and technology, as well as the processes through which institutions manage responses to advances in science and technology. We have purposefully left these definitions broad and inclusive. However, it is apparent to us that there is a need for clearer conceptualisation and articulation of these concepts by key stakeholders at local, national and international level, as part of addressing security challenges presented by this area of innovation.[2]

Introduction to The Techno-Scientific Field of Synthetic Biology

The term 'synthetic biology' has a long history within the biological sciences.[3] However, since the early 2000's the term has become synonymous with work at the cutting-edge of biotechnological innovation. The field is understood by scientists, publics, stakeholders and regulators with reference to past and contemporary fields of innovation, as well as a range of broader trends in innovation (such as convergence between scientific fields).[4] One indicative metric for measuring the growth of synthetic biology as an area of scientific research has been the growth in scientific publications which use the term. In 2003 there were 127 scientific papers which used this term, and the publication rate peaked at around 1000 papers a year in 2012 and 2013.[5]

The emergence of the term in contemporary science and security policy was closely associated with attempts to establish funding for a new research agenda under this label, which began in the US around 2003. The first major investment was in 2006, when the National Science Foundation

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2 Kelle, Dando, and Nixdorff, 'S&T in the Third BWC Inter-Sessional Process: Conceptual Considerations and the 2012 ISP Meetings.'

3 L Campos, 'That Was the Synthetic Biology That Was', in *Synthetic Biology: The Technoscience and Its Societal Consequences*, ed. M. Schmidt et al. (Springer Academic Publishing, Berlin, 2009).

4 See for Example Scientific Committee on Health and Environmental Risks, Scientific Committee on Emerging and Newly Identified Health Risks, and Scientific Committee on Consumer Safety, 'Opinion on Synthetic Biology I Definition', Scientific Committees Opinion (European Commission, 2014), 55–60, http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_044.pdf.

5 Data for Fig. 1 Comes from a Scopus search of titles, abstracts and key words in scientific peer-reviewed articles between 2003-2015. This search excluded social science journals, as well as editorials, letters and other forms of scientific correspondence. The scopus query entered in the search tool available at www.scopus.com: TITLE-ABS KEY (synthetic biology) AND DOCTYPE (ar) AND SUBJAREA (mult OR agri O R bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal OR mult OR ceng OR CHEM OR comp OR eart OR ener OR engi OR e nvi OR mate OR math OR phys) AND PUBYEAR > 2002 AND PUBYEAR < 20 15

provided 10 years of funding at $5 million year for a Synthetic Biology Engineering Research Center (Synberc), based at the University of California, Berkeley, and involving the Massachusetts Institute of Technology, Harvard, Stanford, and the University of San Francisco. It is estimated that between 2008-2014 the US government invested approximately $820 Million into synthetic biology related research. The EU was quick to follow the US and established 27 multi-national collaborative synthetic biology projects.[6] As of December 2012 it was estimated that investment through transnational and bilateral investment mechanisms in the EU totalled € 103 million (~$ 117 million).[7] In Europe at the national level the UK has led the way with investment of around $175 million into inter-disciplinary research centres and networks as well as collaborative initiatives between the academic community and industry.[8]

While the US still leads in terms of synthetic biology publications (see Figure 1)[9] as well as collaboration, publication statistics also provide evidence of the growing internationalisation of the field. In 2013 and 2014 there were more authors publishing synthetic biology research with institutional associations from outside the US than with in it (see Figure 2).[10] Citation data points to

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6 OECD, *Emerging Policy Issues in Synthetic Biology* (OECD Publishing, 2014), 151–152, http://www.keepeek.com/Digital-Asset-Management/oecd/science-and-technology/emerging-policy-issues-in-synthetic-biology_9789264208421-en.

7 ERASynBio, 'Next Steps for European Synthetic Biology: A Strategic Vision from ERASynBio', April 2014, 9, http://www.bbsrc.ac.uk/documents/1404-era-synbio-strategic-vision-pdf/.

8 Synthetic Biology Project and Wilson Center, 'U.S.Trends in Synthetic Biology Research Funding' (online, September 2015), 8, http://www.synbioproject.org/site/assets/files/1386/final_web_print_sept2015.pdf.

9 Data for Fig. 2 Comes from a Scopus search of titles, abstracts and key words in scientific peer-reviewed articles between 2003-2013. This search excluded social science journals, as well as editorials, letters and other forms of scientific correspondence. The scopus query entered in the search tool available at www.scopus.com: TITLE-ABS-KEY (synthetic biology) AND DOCTYPE (ar) AND SUBJAREA (mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal OR mult OR ceng OR CHEM OR comp OR eart OR ener OR engi OR envi OR mate OR math OR phys) AND PUBYEAR < 2014

10 Data for Fig. 3 Comes from a Scopus search of titles, abstracts and key words in scientific peer-reviewed articles published or due for publication between 2013-2014 (date of search 15/12/2014). Excluding research appearing in journals listed under humanities or social science. The scopus query entered in the search tool available at www.scopus.com: (TITLE-ABS-KEY('Synthetic Biology') AND DOCTYPE(ar) AND SUBJAREA(MULT OR AGRI OR BIOC OR IMMU OR NEUR OR PHAR OR MULT OR MEDI OR NURS OR VETE OR DENT OR HEAL OR MULT OR CENG OR CHEM OR COMP OR EART OR ENER OR ENGI OR ENVI OR MATE OR MATH OR PHYS) AND PUBYEAR > 2012 AND PUBYEAR < 2015)

the rapid growth of synthetic biology research in countries such as China, India and Brazil, there is also evidence in growth on the African continent.[11]

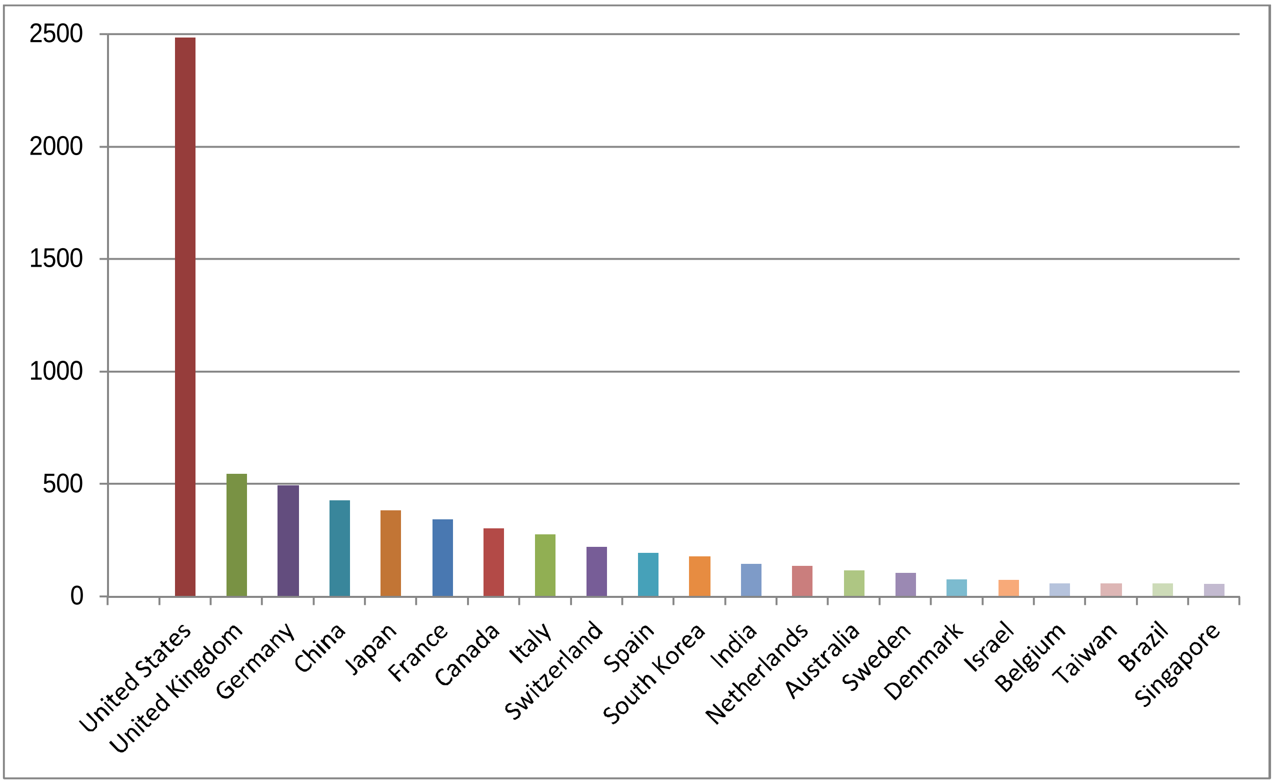

FIGURE 1 A GRAPH SHOWING THE NUMBER OF PUBLICATIONS PER COUNTRY WITH THE TERM 'SYNTHETIC BIOLOGY' APPEARING IN THE TITLE OR PAPER KEY WORDS BETWEEN 2003-2013 (FOR THE TOP 15 COUNTRIES RANKED BY NUMBER OF SYNTHETIC BIOLOGY PUBLICATIONS).

11 Paul Oldham, Stephen Hall, and Geoff Burton, 'Synthetic Biology: Mapping the Scientific Landscape', *PLoS One* 7, no. 4 (2012): 9, http://dx.plos.org/10.1371/journal.pone.0034368.g010.

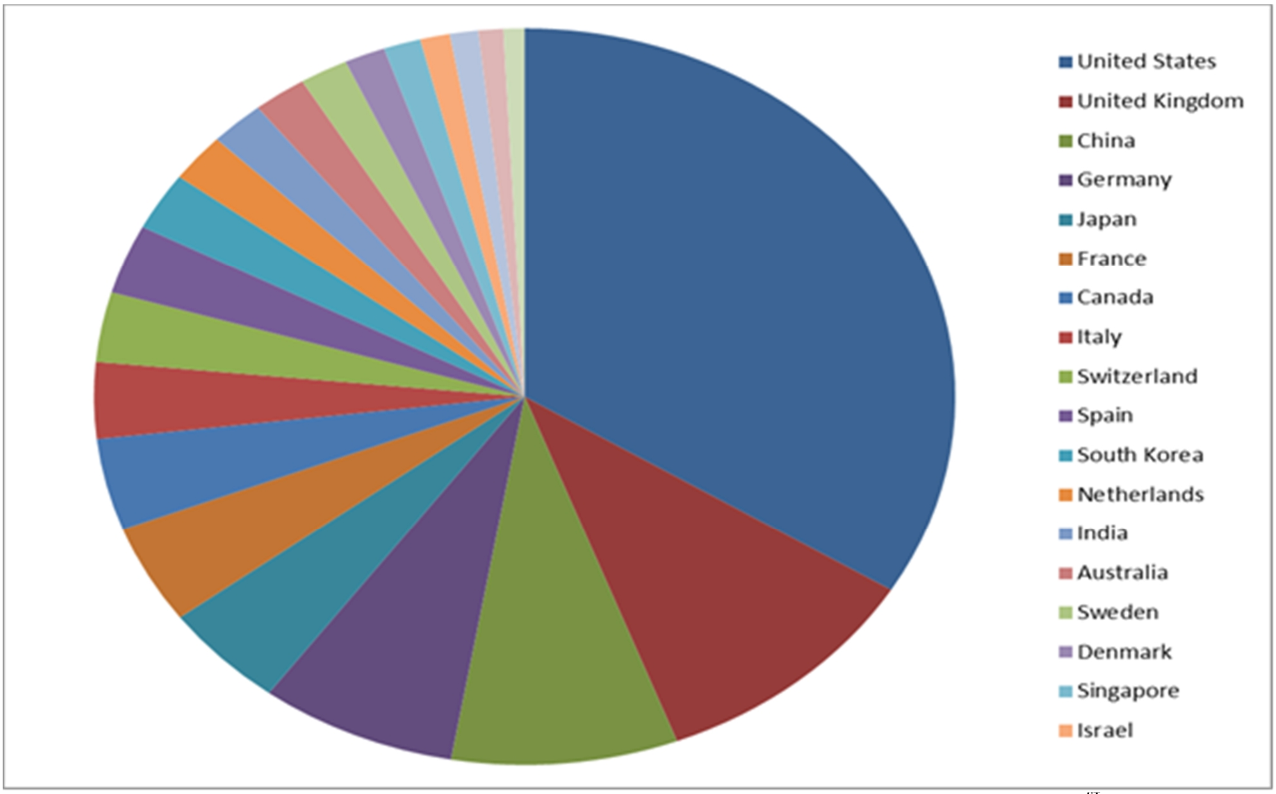

FIGURE 2 A PIE-CHART ILLUSTRATING THE SHARE OF PUBLICATIONS USING THE TERM 'SYNTHETIC BIOLOGY' BETWEEN 1ST JANUARY 2013 AND 31ST DECEMBER 2014 (FOR THE TOP 20 COUNTRIES RANKED BY NUMBER OF SYNTHETIC BIOLOGY PUBLICATIONS)

In each national context, different funding infrastructures and priorities have affected the way in which synthetic biology has been conceived of as a fundable area of scientific research.[12] In addition to this, states each have their own norms in relation to supporting the translation of capacities built in the context of scientific research into marketable applications. This is reflected not only in the private investment profiles in synthetic biology in different national contexts, but also in new and developing national level strategies directed specifically at the field.[13]

A broad range of initiatives are occurring under the label of synthetic biology. With this in mind we have sought to provide a broad-stroke introduction to key developments in three key areas: scientific research, products and services for the scientific sector, and applications.[14]

'Scientific research' relates to work funded by government and other investors directed at building foundational capacities in the field. Such work may have a variety of intellectual goals, and indeed may even seek to redefine the intellectual goals of the field, but is not in of itself a project designed

12 OECD, *Emerging Policy Issues in Synthetic Biology*, 82–83.

13 Ibid., 88–89.

14 However, we acknowledge that such simplified framings of innovation are less than ideal, and agree that in the context of non-proliferation discussions in particular there is the requirement for the development of new models of innovation. On this point I am grateful to Dr Catriona McLeish for comments made at the meeting 'Biological and Chemical Innovation in an Age of Responsibility, Hosted by the University of Bath at the Royal Society 19th-21st November 2014, as well as in personal correspondence.

to create a specific market ready technology or tool as its *primary* outcome. This being said, such work usually seeks to develop the scientific communities' ability to characterise and/or manipulate specific existing biological systems, often with some future potential application(s) in mind. To give an example, in January 2014 Professor Frazer Armstrong at the University of Oxford was awarded a grant for '*proof of principle*' research that would '*step-up*' the development of novel biotechnology concepts that will establish '*solar-cell chloroplast factories*' through, among other things, the metabolic engineering and characterisation of a photosynthetic pathway.[15]

A range of products and services are also being developed for the scientific sector. These are commodified products (such as gene-editing kits and bespoke design services) which are marketed to the scientific community. The commodification of products and services encourages the spread of new techniques and technologies within laboratories.[16]

Finally, 'applications' are marketable technologies for use in a wide range of sectors, from bio-fuel production to healthcare.

Scientific Research

A wide range of definitions of synthetic biology as a field of scientific research have been forthcoming, from scientists, funding agencies, scientific organisations and civil society, and have tended to focus on several defining characteristics of synthetic biology. These definitions each draw attention to a range of institutions, foundational technologies as well as practical and epistemic goals. Indeed, while the majority of publications stemming from synthetic biology research appear in the areas of biochemistry, genetics and molecular biology, publication data reveals the scope of scientific work being published which uses the label (See Figure 3).

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15 BBSRC author, 'Portfolio Analyser', accessed 10 December 2014, http://www.bbsrc.ac.uk/pa/grants/AwardDetails.aspx?FundingReference=BB/M005720/1.

16 It is worth noting however that a) there are various routes and drivers of the uptake of new technologies and approaches within laboratories b) the availability of a product on the market does not mean that it can successfully be used by anyone who wants to use it, or indeed by any laboratory c) there are various types of markets, which are reliant on different types of property rights.

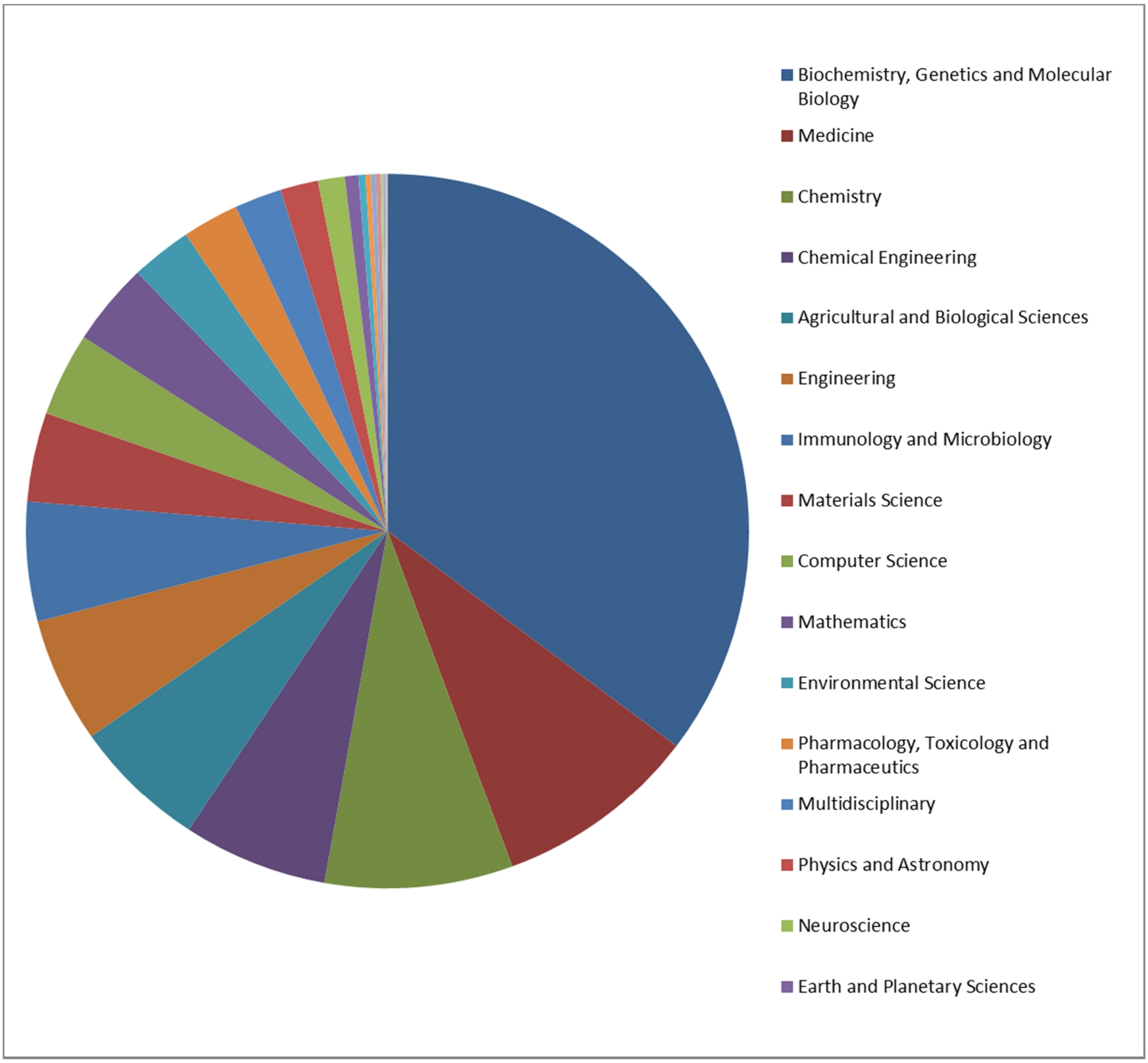

FIGURE 3 A PIE-CHART SHOWING PUBLICATIONS USING THE TERM 'SYNTHETIC BIOLOGY' BETWEEN 2003 AND 2013 (FOR THE TOP 20 TWENTY COUNTRIES RANKED BY NUMBER OF SYNTHETIC BIOLOGY PUBLICATIONS)

Many disagreements about the scope of synthetic biology are political rather than technical in nature. This is because definitions can have consequences, in terms of which research and institutions get funded, as well as how publics and regulators understand the field. This has led to the emergence of numerous definitions of the field; one report, published in 2014, identifies 35 published definitions of synthetic biology. The report found that such definitions were '*focused on conceptual advances within the scientific community*.'[17] In the early years of the field in particular, scientists tried to distinguish synthetic biology through appropriating and articulating aims

[17] OECD, *Emerging Policy Issues in Synthetic Biology*, 6.

traditionally associated with engineering, such as standardization and modularisation.[18] Increasingly however, the field of synthetic biology is understood to have a number of discreet academic sub-fields.[19]

For example, a recent UK funding call identified six sub-fields, which are outlined below:

- Metabolic engineering: Attaining new levels of complexity in modification of biosynthetic pathways for sustainable chemistry
- Regulatory circuits: Inserting well-characterised, modular, artificial networks to provide new functions in cells and organisms
- Orthogonal biosystems: Engineering cells to expand the genetic code to develop new information storage and processing capacity (xeno nucleic acids) and protein engineering
- Bio-nanoscience: Developing molecular-scale motors and other components for cell-based machines or cell-free devices to perform complex new tasks
- Minimal genomes: Identifying the smallest number of parts needed for life as a basis for engineering minimal cell factories for new functions
- Protocells: Using programmable chemical design to produce (semi-)synthetic cells.[20]

Over the previous decade there have been an increasing number of scientific conferences dedicated to synthetic biology; the most notable being the SB x.0 series.[21] Such meetings also provide a forum for investors, academic publishers and companies that provide services and products to the scientific community. The emergence of a young international scientific community has also been greatly facilitated by the annual international Genetically Engineered Machines (iGEM) competition. In 2004, there were 5 teams in the main undergraduate competition.[22] This competition has continued to grow year on year, and the main jamboree has also been expanded to include high-school students. In 2015 there were 280 teams.[23]

The iGEM competition has raised the profile of the field among scientists and policy makers internationally, and a number of comparable competitions run by other organisations have also been

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18 Drew Endy, 'Foundations for Engineering Biology', *Nature* 438, no. 7067 (24 November 2005): 449–53, doi:10.1038/nature04342.

19 Carolyn M C Lam, Miguel Godinho, and Vítor A P Martins, 'An Introduction to Synthetic Biology', in *Synthetic Biology: The Technoscience and Its Societal Consequences*, ed. m Schmidt et al., 2011, 23–48.

20 BBSRC, 'Synthetic Biology ERA-NET - 1st Joint Call', accessed 15 December 2014, http://www.bbsrc.ac.uk/funding/opportunities/2013/era-synbio-call1.aspx.

21 Which were originally organised by the MIT based BioBricks Foundation, which has since become a non-profit organisation based in Cambridge, US.

22 IGEM website http://igem.org/Previous_iGEM_Competitions

23 IGEM website http://2015.igem.org/Main_Page

established.[24] The field also continues to be institutionalised through investment into programs dedicated to synthetic biology post-graduate students.[25] This then provides a strong foot-hold for those involved in the field, in the future of life science research.[26]

PRODUCT AND SERVICE 'TOOLS' FOR THE SYNTHETIC BIOLOGY COMMUNITY

Synthetic biology is producing, as well as importing, a range of techniques and technologies. A recent report identifies three key areas of development: software and bio-informatics design tools; construction tools, including DNA synthesis technologies; and diagnostic tools, such as those used in genetic and protein profiling.[27]

Information on new research techniques can spread through the scientific community through a variety of means, including publications, professional networks and scientific conferences. Likewise, adoption of new methods can be facilitated through physical and virtual collaborations on projects, workshops and other forms of architecture such as information repositories. In addition, there is a global marketplace of both profit making and increasingly non-profit making[28] service and product providers which help facilitate the spread of information on new techniques.

Often it makes practical and economic sense for researchers who want to use a new technique to outsource part of the work required to another organisation or else purchase rather than produce specialist re-agents in-house. As the number of labs wanting to use a technique grows, this often also stimulates commercial investment into the development of complete kits containing relevant materials, technologies and instructions, which reduce the time and understanding needed to carry out certain procedures in-house.

There are several organisations that market themselves as providers of products, tools and services to the synthetic biology community. Some of these companies pre-date the emergence of the field, whereas others are only just attempting to enter the market. Sponsorship and advertising at synthetic

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24 OECD, *Emerging Policy Issues in Synthetic Biology*, 24–26.

25 BBSRC, '2 April 2014 - £12M for Synthetic Biology Facilities and Training', 2014, http://www.bbsrc.ac.uk/news/research-technologies/2014/140402-pr-synthetic-biology-facilities-training.aspx.

26 We are grateful to Dr Piers Millet, for drawing attention to this idea at the meeting 'Biological and Chemical Security in and Age of Responsible innovation' which was held by the Biochemical Security Project (University of Bath) at the Royal Society, London (November 19th -21st 2014).

27 Scientific Committee on Health and Environmental Risks, Scientific Committee on Emerging and Newly Identified Health Risks, and Scientific Committee on Consumer Safety, 'Opinion on Synthetic Biology I Definition', 13–14.

28 For Example, Add-gene specialises in providing plasmids via-mail order for a fee, for use by researchers. Add-gene maintains a database of plasmids, which have been developed and deposited by researchers, so that they can be used more easily by others.

biology events gives some indication of the scope of organisations that use the banner of synthetic biology in relation to their products. At Synthetic Biology 6.0 for example, held in London in 2013, sponsors and exhibitors included larger firms such as Agilent Technologies, which provides a wide range of laboratory equipment, products and services.[29] Some of these firms, such as Life Technologies, market specific products under the label of synthetic biology. This includes a series of services carried out under the GeneART trademark.[30] A number of newer companies, such as Synthetic Genomics inc, which provides a wide range of design and synthetises services, are spin-off companies based on capacities built in the context of federally and privately funded synthetic biology research.[31] This emphasises the close working relationships between some industries and some leading researchers. A testament to this is the way in which companies have been quick to offer services based on very recently developed lab techniques, such as the CRISPR technique for gene-editing.[32] A brief time-line of this example is provided on the next page.

29 Agilent Website http://www.agilent.com/home

30 Synthesis Website http://www.synthesis.cc/2010/04/life-technologies-buys-geneart.html

31 SGIDA Website https://sgidna.com/founders.html

32 See for example Heidi Ledford, 'CRISPR, the Disruptor', *Nature* 522, no. 7554 (3 June 2015): 20–24, doi:10.1038/522020a.

The rapid spread of innovation: The case of CRISPR editing

The first academic papers presenting CRISPR inspired editing were published in January 2013.

In April 2014 a patent covering the CRISPR technique was granted to the Broad Institute, a Harvard-MIT genomic science institute. The patents have coincided with investment into companies affiliated with the inventors who hold the patent, as well as those likely to be granted licences to use the technique for commercial purposes, and further research into using the technique.

By August 2013, do-it-yourself reagent kits for the CRISPR technique were already available, as were all-in-one ready to use Cas9 and guide RNA (gRNA) expression plasmids. Currently, a number of companies also offer a range of CRISPR based services (see table below), one such company for example offers all-in-one expression vector, Cas9 mRNA, and complete engineering service. This means that within only two years of the technique coming to wider attention, a range of CRISPR based services and products are available to laboratories around the world. It is worth also noting for example, that a substantial number of academic papers have already been published which discuss the application and refinement of the technique.

Company (location)	Product description
Applied StemCells (Menlo Park, California)	Genome engineering, gene editing and knock-in cell lines
GenScript (Piscataway, New Jersey)	gRNA design, transfection and cell pool evaluation, single-cell clone generation and validation
GeneCopoeia (Rockville, Maryland)	Research tools, Cas9 nuclease expression, genome-CRISPR sgRNA design and cloning services
Horizon Discovery	Gene-editing tools, validated gRNAs, Cas9 vectors, cell line generation kit, delivery vectors
Life Technologies (Carlsbad, California)	CRISPR Nuclease Vector Reporter Kit, genome-CRISPR sgRNA design and cloning services
OriGene (Rockville, Maryland)	CRISPR cloning kits, CRISPR-Cas9 custom services
Sage Labs	Transgenic animal models, knockout, gene replacement, targeted transgenics
Sigma-Aldrich (St. Louis)	Plasmid expressing Cas9, GFP and customizable gRNA under U6 pol III promoter
ToolGen	Custom-designed crRNA for target with tracrRNA and Cas expression systems

Table from: Baker, Monya. 2014. “Gene Editing at CRISPR Speed.” *Nature Biotechnology* 32 (4): 309–12. doi:10.1038/nbt.2863.

The CRISPR example goes to show the way in which technologies and techniques developed in the context of scientific research can be quickly developed, shared, and commercialised enabling the adoption of these approaches in laboratories internationally.

Synthetic Biology and Applications

A wide range of application have been discussed over the previous decade including fine chemical production, drug and vaccine development, bio-fuel production as well as a range of agricultural applications.[33] While many products are still under development in these sectors, several synthetic biology based products have already entered the market, or are in the process of being developed for the marketplace. The earliest products linked with this field have been those that have involved the engineering of yeast to enable the industrial scale production of fine chemicals. The most established product is an Artemisinin based drug, which is used to treat Malaria.[34] Synthetic biology techniques were utilised to engineer yeast to produce a precursor of the active component, which was traditionally obtained from more expensive and less reliable natural resources.[35] More recently, a synthetic biology based company also announced the launch of the first synthetically produced food additive.[36] Currently, a search of Synthetic Biology Project inventory lists 51 synthetic biology products which are on, or close to entering the market.[37]

States are increasingly prioritising investment into biotechnology,[38] and the field of synthetic biology (however that is understood) has been a key component of such investment in recent years.[39] As part of this work, national strategies have been developed to help get discoveries from the laboratory to the market. In the case of biologically mediated synthesis of chemicals for example, increasingly the question isn't whether it is possible to engineer a microorganism to

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33 James Newcomb, Robert Carlson, and Stephen Aldrich, 'Genome Synthesis and Design Futures: Implications for the U.S. Economy' (Cambridge, MA, US: Bio-era Economic Research Associates, 2007), 71–101; Ahmad S. Khalil and James J. Collins, 'Synthetic Biology: Applications Come of Age', *Nature Reviews Genetics* 11, no. 5 (5 January 2010): 367–79, doi:10.1038/nrg2775; For a recent substantive review see also OECD, *Emerging Policy Issues in Synthetic Biology*, 31–54.

34 Project information available on the Amyris website: https://amyris.com/collaborations/artemisinin/
Mark Peplow, 'Malaria Drug Made in Yeast Causes Market Ferment', *Nature* 494, no. 7436 (13 February 2013): 160–61, doi:10.1038/494160a.

36 Erika Check Hayden, 'Synthetic-Biology Firms Shift Focus', *Nature* 505, no. 7485 (29 January 2014): 598–598, doi:10.1038/505598a.

37 Search carried out 07/12/2015 at http://www.synbioproject.org/cpi/

38 OECD, 'The Bioeconomy to 2030:designing the Policy Agenda', 2009, http://www.oecd.org/futures/long-termtechnologicalsocietalchallenges/42837897.pdf; The White House, 'National Bioeconomy Blueprint' (Washington, D.C., 2012), http://www.whitehouse.gov/sites/default/files/microsites/ostp/national_bioeconomy_blueprint_april_2012.pdf.

39 See for example OECD, *Emerging Policy Issues in Synthetic Biology*.

produce a compound, or key precursor, but whether it can be made economically viable. National strategies have also addressed the need to engage regulators early in the process, to help reduce uncertainty for investors and the public.

THE SIGNIFICANCE OF SYNTHETIC BIOLOGY AS A BIOSECURITY 'TEST-BED'

The discussions of security concerns related to synthetic biology actually pre-date the first major investments into the field. Some of these discussions have been largely speculative, others however have been tied to more pro-active and pre-emptive approaches to horizon scanning and oversight. The first synthetic biology conference was held at MIT in June 2004, and even at this event security concerns related to emerging foundational DNA synthesis technologies were being discussed.[40] This reflected the broader political environment at the time, in which security concerns related to life science research were being given significant attention particularly in the US.[41] Indeed, such anxieties meant the US National Science Foundation stipulated that misuse concerns must be addressed in the projects it funded.[42] As a result, such concerns came to wider public attention, and also came to the attention to the broader national security and non-proliferation policy communities.[43] When European funders looked to invest into the field, these security concerns were also addressed European biotechnology assessment; in addition to more traditional European concerns about safety.[44] It was also around this time that concerns about amateur biology[45] became

40 Robert Carlson, 'Synthetic Biology 1.0', *Future Brief*, 2005, http://www.futurebrief.com/robertcarlsonbio001.asp.

41 Erika Check, 'Poliovirus Advance Sparks Fears of Data Curbs', *Nature* 418, no. 6895 (18 July 2002): 265, doi:10.1038/418265a; E. Check, 'US Officials Urge Biologists to Vet Publications for Bioterror Risk.', *Nature* 421, no. 6920 (2003): 197; National Research Council, *Biotechnology Research in an Age of Terrorism* (Washington, D.C.: The National Academies Press, 2004).

42 Paul Rabinow and Gaymon Bennett, *Designing Human Practices: An Experiment With Synthetic Biology* (Chicago: University of Chicago Press, 2012), 17.

43 M. S Garfinkel et al., 'Synthetic Genomics: Options for Governance', *Industrial Biotechnology* 3, no. 4 (2007): 333–65; NSABB, *Addressing Biosecurity Concerns Related to Synthetic Biology* (Washington, D.C., 2010), http://osp.od.nih.gov/sites/default/files/resources/NSABB%20SynBio%20DRAFT%20Report-FINAL%20%282%29_6-7-10.pdf.

44 'It has been suggested that, in addition to abuses of synthetic biology at the scales of organized terrorist groups or even biological warfare initiatives at a national level, there is a danger of the development of a "bio-hacker" culture, in which lone individuals develop dangerous organisms much as they currently create computer viruses' NEST High-Level Expert Group, *Synthetic Biology Applying Engineering to Biology: Report of a NEST High-Level Expert Group* (Luxembourg: European Commission, 2005), 17, http://www.bsse.ethz.ch/bpl/publications/nestreport.pdf; Balmer and Martin, *Synthetic Biology: Social and Ethical Challenges*.

embroiled with discussions about synthetic biology.[46] Such discussions were associated with a number of initiatives directed at identifying and mitigating potential security concerns associated with synthetic biology. These have included; horizon scanning and other forms of expert review and assessment, which have considered security concerns and the scope and potential short comings of existing regulatory and oversight systems,[47] education and awareness raising within the synthetic biology community by law enforcement[48] and social scientists,[49] as well as engagement with biosecurity issues as part of the ethical, safety and security review of projects entered into the iGEM competition.[50] A secondary effect of such engagement has been the emergence of an informal network of scientists, policy shapers and academics with expertise on biosecurity issues in relation to synthetic biology. These initiatives have created a large literature on the field and its potential security implications.

There are potentially several types of lessons that can be taken from such experiences. First, experiments with anticipatory governance of security concerns have flagged many of the conceptual, practical and political challenges which will remain relevant to future work in this

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45 Catherine Jefferson, 'The Growth of Amateur Biology: A Dual Use Governance Challenge?', Biochemical Security 2030 Project Paper Series (Bath: University of Bath, 2014), http://biochemsec2030.org/policy-outputs/.

46 NEST High-Level Expert Group, 'Synthetic Biology Applying Engineering to Biology: Report of a NEST High-Level Expert Group', 17.

47 For Example S. M Maurer, K. V Lucas, and S. Terrell, 'From Understanding to Action: Community-Based Options for Improving Safety and Security in Synthetic Biology', *University of California, Berkeley. Draft* 1 (2006); Garfinkel et al., 'Synthetic Genomics'; Newcomb, Carlson, and Aldrich, 'Genome Synthesis and Design Futures: Implications for the U.S. Economy'; NSABB, 'Addressing Biosecurity Concerns Related to Synthetic Biology'; Presidential Commission for the Study of Bioethical Issues, 'New Directions: The Ethics of Synthetic Biology and Emerging Technologies', 2010, http://www.bioethics.gov/documents/synthetic-biology/PCSBI-Synthetic-Biology-Report-12.16.10.pdf.

48 Edward W. Lempinen, 'Outreach to Biotech Researchers and DIY Biologists', *AAAS: News*, April 2011, http://www.aaas.org/news/fbi-aaas-collaborate-ambitious-outreach-biotech-researchers-and-diy-biologists.

49 Brett Edwards and Alexander Kelle, 'A Life Scientist, an Engineer and a Social Scientist Walk into a Lab: Challenges of Dual-Use Engagement and Education in Synthetic Biology', *Medicine, Conflict and Survival* 28, no. 1 (2012): 5–18, doi:10.1080/13623699.2012.658659; Rabinow and Bennett, *Designing Human Practices*; Catherine Jefferson, Filippa Lentzos, and Claire Marris, 'Synthetic Biology and Biosecurity: Challenging the "myths"', *Infectious Diseases* 2 (2014): 115, doi:10.3389/fpubh.2014.00115.

50 iGEM Website http://2014.igem.org/Tracks/Policy_Practices

area.[51] Recently, Megan Palmer, who worked as Deputy Director of Human Practices at National Science Foundation (NSF) Synthetic Biology Engineering Research Center (Synberc) noted:

> *'A core challenge for realizing benefits, and mitigating risks, of advances in biotechnology is equipping increasingly diverse and distributed practitioner communities with the capacity for effective foresight. Individuals must become increasingly adept at assessing the drivers and potential consequences of their work, and aware of their roles and responsibilities in shaping outcomes. Creating an environment that enables such assessment requires institutional infrastructures that can share information and develop norms on global scales. Effective institutions require strong leaders that value not just technical prowess but deep social engagement, accountable organizational structures, and mechanisms to efficiently monitor and share performance to support organizational learning and adaptation. Developing more effective communication between stakeholders with complementary information, expertise and interests is essential. There is a concerning dearth of knowledge on how communities might prepare for and respond to the inevitable risks and surprises posed by manipulating the living world. Attention to social and organizational dimensions will be critical to maturing our systems of work and oversight'*[52]

In addition to these challenges, it is also not currently clear how capacities and awareness built in security initiatives directed at the synthetic biology research community, in the US in particular, will translate into the emergence of responsible innovation models within industry going forward in the US and elsewhere. This is because initiatives directed at this community have primarily dealt with a relatively narrow set of issues relevant to research, such as laboratory safety and laboratory security, ethics review, as well as regulations directed at Genetically Modified Organisms. The translation of discoveries in this field into applications involves significant shifts in terms geography and physical scale, leading to different types of security concerns which are subject to different pre-existing and *sui generis* governance systems. This includes concerns about emergent synthetic biology facilitated markets; both licit and illicit. For example, over the previous decade there have been initiatives directed at ensuring responsibility in industries which synthesise and ship genetic material to customers. This has included the establishment of industry screening standards for orders.[53] However, there are a range of research related products and technologies which might also raise potential concerns. For example, a recent study by Raymond Zilinskas and Philippe

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51 The most in-depth analysis of this area is Rabinow and Bennett, *Designing Human Practices*; See also Stephen Maurer, 'End of the Beginning or Beginning of the End? Synthetic Biology's Stalled Security Agenda and the Prospects for Restarting It', *Valparaiso University Law Review* 45, no. 4 (19 September 2011): 73–132; Edwards and Kelle, 'A Life Scientist, an Engineer and a Social Scientist Walk into a Lab'; Brett Edwards, 'Taking Stock of Security Concerns Related to Synthetic Biology in an Age of Responsible Innovation', *Infectious Diseases* 2 (2014): 79, doi:10.3389/fpubh.2014.00079.

52 Megan Palmer, 'SynBERC: Correspondence with Brett Edwards', 12 2014, On file with author.

53 Maurer, 'End of the Beginning or Beginning of the End?'

Mauger has examined industry practices in relation to established biotechnologies which are on Australia Group export lists, as well as cutting-edge technologies which raise potential concerns about the coverage of existing lists. This includes synthetic biology based kits, which are widely available online. In relation to one of the kits they examined, they note that:

> ‘*While kits like this one provide novices with the means to create genetic constructions with quite limited functional capabilities, the pace of technology advancement in this area of science suggests that within 10 years novices will be afforded many more opportunities for creating recombinant organisms with far more diverse capabilities.*’[54]

In addition, recent discussions stimulated by the development of a new process for opiate synthesis aimed at increasing global access to opiate based medicine, point to the ways in which advances might fundamentally undermine existing approaches to control. As Kenneth Oye et al. note in a paper appearing in Nature:

> ‘*Yeast-based production of opiates could provide an alternative system for current criminal networks, particularly in North America and Europe, where the drugs are in high demand. Because yeast is easy to conceal, grow and transport, criminal syndicates and law-enforcement agencies would have difficulty controlling the distribution of an opiate-producing yeast strain. All told, decentralized and localized production would almost certainly reduce the cost and increase the availability of illegal opiates — substantially worsening a worldwide problem*’[55]

While researchers involved in this work have argued and experimentally demonstrated that the existing laboratory strains cannot produce key pre-cursors outside of laboratory conditions,[56] this is another example of how cutting-edge fields such as synthetic biology become sites for the discussion of forward looking concerns about biotechnology and the best approaches to respond to them.

This section has demonstrated that synthetic biology has already been the focus of substantial discussion and review, particularly in the US and Europe, and it might then be

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54 Raymond A. Zilinskas and Phillipe Mauger, ‘Biotechnology E-Commerce: A Disruptive Challenge to Biological Arms Control’, CNS Occasional Paper (Middlebury Institute of International Studies: James Martin Center for Nonproliferation Studies, March 2015), 35, http://www.nonproliferation.org/wp-content/uploads/2015/06/biotech_ecommerce.pdf.

55 Kenneth A. Oye, J. Chappell H. Lawson, and Tania Bubela, ‘Drugs: Regulate “Home-Brew” Opiates’, Nature 521, no. 7552 (18 May 2015): 281–83, doi:10.1038/521281a.

56 Drew Endy, Stephanie Galanie, and Christina D. Smolke, ‘Complete Absence of Thebaine Biosynthesis under Home-Brew Fermentation Conditions’, bioRxiv, 2015, 024299, http://biorxiv.org/content/early/2015/08/13/024299.

time to reflect on the broader implications of these experiences for thinking about universal principles for good governance in relation to cutting-edge advances in research and industry. In the following sections, we reflect on the extent to which this need has been recognised in existing reviews in the context of the BTWC and CWC.

Synthetic Biology at the CWC and BTWC

Now that the techno-scientific field of synthetic biology has been introduced in general terms we examine how synthetic biology has been addressed in the context of the CWC and BTWC. We begin by outlining the key ways in which the term has been utilised in recent years by States Parties in the context of the BTWC and CWC official documentation. This then allows for a critical reflection on the way in which the field has been discussed so far within these regimes.

CWC S&T Review Process

Within the CWC there are two central aspects of S&T review. The first is the Science Advisory Board (SAB), which comprises of 25 experts serving in their individual capacity. The SAB generally meets two to three times a year and produces reports of these sessions. The SAB reports to the Director-General, who then submits these reports, alongside his own responses, to the Executive Council. The SAB can also establish Temporary Working Groups (TWGs), whose findings are communicated via its own meeting reports and are also presented within SAB reports to the Executive Council. Every five years, the SAB also prepares a larger report for submission to the review conference. This process involves contribution from civil society, primarily through workshops, as well as reports produced by the International Union of Pure and Applied Chemistry.[57]

BTWC S&T Review Process

Historically, S&T engagement in the BTWC has been limited to ad hoc discussion such as the VEREX sessions in the early 1990s on the one hand, and the quinquennial BTWC S&T review which form part of the broader review conference process and involved the submission of national S&T papers from Depositories and later States Parties. Such submissions have been somewhat organic and taken different forms over the course of the evolution of the convention, yet two consistent features are the relatively limited number of countries that contribute and the comparatively limited discussion time allocated to these papers. In early review conferences there was no time allocated specifically to the issue of S&T advances during formal sessions, and

[57] For further information see Leiv K. Sydnes, 'IUPAC, OPCW, and the Chemical Weapons Convention', *CHEMISTRY International* 35 (2013), http://www.degruyter.com/view/j/ci.2013.35.issue-4/ci.2013.35.4.4/ci.2013.35.4.4.xml.

discussions where they did occur, tended to focus on the potential impact of S&T developments on the scope of the convention in terms of Article I, rather than the broader implications for the implementation of the convention.[58] Since the Fifth Review Conference, the Inter-Sessional Process (ISP) has increasingly become a forum for discussion of S&T developments albeit in a rather limited fashion. The ISP, which is, in its present form, largely open to observation by non-governmental organizations, has fostered contributions on S&T topics from a wide range of stakeholders, though presentations made at the Meeting of Experts, as well as through side events held at Inter-Sessional Meetings. External bodies within the international scientific community have also held expert meetings bringing together diplomats and scientist to discuss S&T of relevance to the BTWC and produced reports for the benefit of the convention.[59] Since its establishment following the Sixth Review Conference of 2006, the Implementation Support Unit (ISU) has also produced a number of background documents on science and technology for Meetings of Experts (MXs), Meetings of States Parties (MSPs) and the Seventh Review Conference, which provide a concise, coherent and publicly available overview of developments which are of potential relevance to the convention.

During the Seventh Review Conference a new model for formal integration of discussion on S&T in the ISP was agreed. S&T was identified as a standing agenda item for recurrent discussion and several recurring annual topics of discussion were agreed. Each of these was conceivably relevant to the identification, management and mitigation of dual-use issues at national and international level. They included, for example '*new science and technology developments that have potential for uses contrary to the convention*', as well as '*voluntary codes of conduct and other measures to encourage responsible conduct by scientists, academia and industry*'. However, as has been noted elsewhere, the structure settled on at the Seventh Review Conference for the third ISP remains of limited use as a means for agreement on action.[60] It is currently unclear how the formal process will

58 Caitríona McLeish and James Revill, 'Reviewing Science and Technology in the Context of the Biological Weapons Convention' (presented at the 31st Workshop of the Pugwash Study Group on Implementation of the CBW Conventions Geneva, Geneva, 2010); Caitríona McLeish, 'Implications of Bioscience and Technology Advances for the BTWC', *EU Non-Proliferation Consortium* 4 (December 2011): 2–3, http://www.nonproliferation.eu/documents/nonproliferationpapers/caitrinoamcleish4ed77f84a1e4f.pdf.

59 See for example Katherine Bowman et al., *Trends in Science and Technology Relevant to the Biological and Toxin Weapons Convention: Summary of an International Workshop: October 31 to November 3, 2010, Beijing, China* (National Academies Press, 2011), http://www.nap.edu/catalog/13113/trends-in-science-and-technology-relevant-to-the-biological-and-toxin-weapons-convention.

60 Malcolm Dando, 'To What Extent Was The Review Of Science And Technology Made More Effective And Efficient At The 2013 Meeting Of BTWC States Parties?', Biochemical

look following the next review conference, although it seems likely that a number of states are pushing for improved capacities in this area. At the 2015 MX, for example, the Swiss delegation submitted a working paper[61] which outlined some initial ideas for improving this process. It is apparent that any change should aim to maximise scientific community input into this process, and build upon and supplement capacities and networks developed by scientific organisations which already support the work of the convention. However, the future of such engagement is dependent on political and funding issues.

SYNTHETIC BIOLOGY AND THE BTWC

Early investment into the development of a field of synthetic biology occurred in US between the Fifth and Sixth Review Conference. Synthetic biology is first referred to explicitly in a background information document on advances in science and technology produced in the run up to the Sixth Review Conference. This initial review, focused on the aims of the early US based synthetic biology community to apply engineering principles to biology.[62] Since this time the field has continued to grow in terms of scope, participation and geography. The continued development of this field in the context of the BTWC and this has been reflected in the ISU document produced for the 2011 Review Conference, which stated that

> *'Biological engineering, or synthetic biology, has advanced considerably since the last review conference. Industry is becoming increasingly interested in these approaches. There has been a significant increase in the biological complexity of the biological systems and networks that can be engineered'*[63]

The growing significance of synthetic biology for the BTWC has also been reflected in State Party submissions during the Second ISP, Seventh Review Conference and Third ISP. During the Seventh Review Conference, various aspects of synthetic biology were referred to by State Parties in working papers submissions, including some which pointed to potential military interest in the

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Security Project 2030 Paper Series (University of Bath, 2014), http://biochemsec2030.org/policy-outputs/.

61 Switzerland, BTWC/MSP/2015/MX/WP.11 http://www.unog.ch/80256EDD006B8954/%28httpAssets%29/E4BDDFC6FA67EB77C1257E9A0041E000/$file/BTWC_MSP_2015_MX_WP11.pdf

62 BTWC Secretariat, 'Backgroud Information Document on New Scientific and Technological Developments Relevant to the Convention' (BTWC, September 2006), 15, http://daccess-dds-ny.un.org/doc/UNDOC/GEN/G06/643/31/PDF/G0664331.pdf?OpenElement.

63 Implementation Support Unit, 'New Scientific and Technological Developments Relevant to the Convention' (BTWC, October 2011), 6, http://daccess-dds-ny.un.org/doc/UNDOC/GEN/G11/640/10/PDF/G1164010.pdf?OpenElement.

field,[64] existing approaches to identifying and responding to security risks associated with the field[65] concerns that synthetic biology could undermine existing select-agent oversight systems and make it easier to produce such pathogens,[66] the issue of convergence and the work of the BTWC and CWC,[67] the pace of developments in synthetic biology. Perhaps the most comprehensive review was produced by the UK, which considered how synthetic biology potentially impacted on a number of articles across the treaty, including Articles I, III and X.[68]

Such submissions are by no means monolithic in their assessment, but have repeatedly ascribed significance to various aspects of the field, in relation to its current capacities and future promise. This includes emphasis on the impacts of improved foundation capacities in gene-synthesis in the life sciences, the spread of such capacities internationally[69] and the potential for new applications in a wide range of sectors including healthcare.[70] At the same time, several States Parties have also pointed to how techniques and foundational technologies may also have a dual-use potential. For example, the delegations for the Netherlands and the 2012 MX stated that:

> *'When one is capable of designing a viral genome, one could also introduce mutations which are harmful they could possibly make a virus more pathogenic. …..In this respect applying the techniques of synthetic biology, the design and synthesis of a viral genome could be of dual use'*[71]

Likewise, as noted in a ISU background information document for the Seventh Review Conference, it is China's position that:

> *With the spread of synthetic biology, some small scale research groups and even some individuals are now able to make the deadly Ebola and smallpox viruses and even some viruses against which all drugs are ineffective, thus making it much harder to counter bioterrorism. Furthermore, it has become much easier to obtain sensitive information. Using publicly available DNA sequences, terrorists can*

64 China, Implementation Support Unit, *New Scientific and Technological Developments Relevant to the Convention (Addendum- Submissions from States Parties* (BTWC, October 2011), 7, http://daccess-dds-ny.un.org/doc/UNDOC/GEN/G11/640/10/PDF/G1164010.pdf?OpenElement.

65 China, Netherlands ibid., 8–9, 9–10.

66 South Africa ibid., 14.

67 United Kingdom ibid., 21.

68 United Kingdom ibid., 25.

69 Netherlands, 'Opening Statement from The Netherlands' (presented at the UN BTWC Meeting of Experts 2012, Geneva, August 2012), http://www.unog.ch/80256EE600585943/%28httpPages%29/26E4793F76DAF81EC1257A87002C4700?OpenDocument.

70 Netherlands' Opening statment from the Netherlands' ibid.

71 Ibid.

quickly synthesize pathogenic microbes that had previously been eradicated or give existing ones new pathogenic properties.[72]

Such claims however, whilst perhaps not untrue *per se*, tend to focus on worst case hypothesis and do not involve assessments of the likelihood or feasibility of such misuse. This perhaps suggests that in the BTWC context, synthetic biology is generally discussed as shorthand for advanced biology; and is perhaps an 'emblematic' label for advanced biotechnology, as well as the opportunities and challenges that such advances entail.

Indeed, this perhaps accounts for why synthetic biology is also increasingly utilised with reference to other issues relevant to the BTWC. This includes Article X issues for example. At the 2013 MX, Iran stated on behalf of NAM countries that:

> *'Advances in enabling technologies like bioinformatics; computational biology; DNA microarrays; gene synthesis technology; high-throughput mass spectrometry; high- throughput sequencing; nanotechnology; synthetic biology; systems biology; and whole- genome directed evolution are critical for future life sciences research and development. These enabling technologies have many benefits in faster, cheaper, and easier application of biological science and technology for both public health and security purposes, increased capacity and better understanding of disease and healthcare technologies by more people in more locations throughout the world. Furthermore new science and technology developments have many potential benefits for the Convention in improved health care, increasing capacity to diagnose and treat diseases, more efficient food production, more renewable energy resources and better pollution management. In this regard [there is a need for] a plan for active and fullest exchange of knowledge and technology in areas related to enabling and new technologies between developed and developing countries'*[73]

Likewise, discussions about synthetic biology have also become associated with the reassertion of the need for both transparency and national level risk management and oversight systems. At the 2014 MX for example, Pakistan speaking on behalf of non-aligned (NAM) States Parties, stated that:

> *'The recent advances in synthetic biology raise immediate concerns related to ethics, safety and security. In this regard, States should employ utmost transparency and confidence building measures during all their activities related to synthetic biology. There is also a need for strict regulation on the development of synthetic biology, to ensure that it does not lead to any concerns related to safety and security as well as*

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72 Biological and Toxin Weapons Convention Implimentation Support Unit, 'New Scientific and Technological Developments Relevant to the Convention – Addendum (Submissions from States Parties)' (Geneva, 12 January 2011), 1, http://daccess-dds-ny.un.org/doc/UNDOC/GEN/G12/600/29/PDF/G1260029.pdf?OpenElement.

73 Islamic Republic of Iran, 'Opening Statement from Islamic Republic of Iran on Behalf Of the Group of Non-Aligned and Other States' (presented at the UN BTWC 2013 Meeting of Experts, Geneva, August 2013), http://www.unog.ch/__80256ee600585943.nsf/%28httpPages%29/eed3e63397c2144bc1257bf80054fe12?OpenDocument&ExpandSection=6#_Section6.

incidents of proliferation that have no justification for prophylactic, protective or other peaceful purposes'[74]

Such a position on synthetic biology is perhaps more general reflection of NAM policy which places great emphasis on peaceful cooperation and has long challenged the restriction of the movement of such technologies in the name of security.[75] Yet it also highlights how advances in synthetic biology are already being understood to have impacts across a number of articles of the treaty.[76] The field also continues to be referred to in technical presentations given at Inter-Sessional Meetings.

In terms of raising awareness about the potential implications of this field for the future of BW non-proliferation this is certainly a promising development. However, existing discussions of synthetic biology in the BTWC in Geneva do not equate to a comprehensive and systematic review of the relevance of developments of this, and related fields, to the treaty. Nor do they equate to discussions focused on agreeing practical steps in dealing with the challenges raised by the field. We return to this issue in our conclusions and recommendations.

SYNTHETIC BIOLOGY AND THE CWC

The term 'synthetic biology' is not explicitly discussed in the reports of the SAB until 2007.[77] However, the SAB has been discussing many trends, such as the convergence between scientific disciplines, which synthetic biology which has come to symbolize for well over a decade. For example, in 2003, a note by the Director-General on the work of the SAB in the run up to the first review conference states:

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74 Pakistan, 'Opening Statement from Pakistan' (UN BTWC Meeting of Experts 2013, Geneva, August 2013), http://www.unog.ch/__80256ee600585943.nsf/%28httpPages%29/eed3e63397c2144bc1257bf80054fe12?OpenDocument&ExpandSection=6#_Section6.

75 Speaking on behalf of NAM for example at the 2014 MX, Pakistan stated that: 'the potential dual-use nature of emerging technologies in itself should not be used as a pretext for proscribing or restricting their availability to developing countries for peaceful purposes'. Pakistan, 'Opening Statement from Pakistan' (UN BTWC Meeting of Experts 2014, Geneva, August 2014), http://www.unog.ch/80256EE600585943/%28httpPages%29/F837B6E7A401A21CC1257A150050CB2A?OpenDocument.

76 See for Example Kai Ilchman et al., 'Synthetic Biology & the BTWC', Briefing Note, Briefing Note Series (Harvard Sussex Program, 2011), http://hsp.sussex.ac.uk/sandtreviews/; Bowman et al., *Trends in Science and Technology Relevant to the Biological and Toxin Weapons Convention*.

77 The field is referred to in reference to a forthcoming IUPAC conference under preparation (The Impact of Advances in Science and Technology on the Chemical Weapons Convention, Zagreb, Croatia, 22 to 25 April 2007) Scientific Advisory Board, *Report of the Ninth Session of the Scientific Advisory Board*, February 2007, 5, http://www.opcw.org/fileadmin/OPCW/SAB/en/sab-901_e_.pdf.

'Advances in molecular biology (such as genomics and proteomics are creating new opportunities both to design new biologically active chemicals and to develop processes to synthesise such chemicals using enzymes or cell-based systems. The rapid pace of developments in the biomolecular sciences, coupled with advances in chemical synthesis, increase the possibility that new toxic chemicals will be found that may have properties that would make them suitable candidates for CW.'[78]

In addition, concerns about the potential implications for the convention for biologically mediated production, and specifically concerns about the industrialisation of biotechnologically mediated chemical production, were being discussed as early as 1994 in the process of determining interpretations of the Convention.[79] As Trapp highlights, in 1999, the SAB addressed issues related to biologically mediated synthesis when providing advice on whether

'the term "production by synthesis" used in the CWC's provisions pertaining to "other chemical production facilities" (i.e., chemical plant sites that that produce unscheduled discrete organic chemicals or unscheduled Discreet Organic Chemicals) would also include manufacturing processes that involved biological or biologically-mediated processes.[80]

As Trapp goes on to note, it is clear that all scheduled agents covered by the treaty fall within its scope regardless of the means through which they are produced; however what is less clear is how the regime will respond to the emergence of new types of bio-based chemical production facility which may foreseeably require inspection.[81] More broadly, in 2000, the Report of the Third Session of the Scientific Advisory Board to the OPCW identified a wider range of ways in which developments in biology and chemistry, and in particular the interface between them, could impact on the regime, stating that:

'The Board considered that it would be useful to identify areas of science and technology that should be analysed in some detail, with respect to how current developments will impact on the scientific foundations of the Convention. Areas that may deserve detailed study could include chemical analysis, equipment and instruments, biosynthesis and other trends in chemical manufacturing, biotechnology, remote sensing, nano-technology (both with respect to analysis and

78 Director General, *Report of the Scientific Advisory Board on Developments in Science and Technology*, Note by Director General to First Review Conference (OPCW, April 2003),14.

79 Harvard Sussex Program. (1994). Building the Organization for the Prohibition of Chemical Weapons. *Chemical Weap*, (26), 7–14.

80 Ralf Trapp, 'Convergence at the Intersection of Chemistry and Biology- Implications for the Regime Prohibiting Chemical and Biological Weapons', Biochemical Security Project Paper Series (Bath: University of Bath, July 2014), 12–13, http://biochemsec2030.org/policy-outputs/.

81 Ibid.

synthesis), and bioassays. The Board considered that, as a next step, the areas to be studied in detail need to be further clarified.'[82]

Despite the discussion of trends in science and biotechnology that are fundamentally associated with the concept of synthetic biology, it would not be until November 2011 that any specific action was agreed upon. The SAB recommended that a detailed technical feasibility study should be conducted to examine the potential implications of synthetic biology for the production of Saxitoxin or Ricin.[83] While synthetic biology was only mentioned in relation to this recommendation, other recommendations also spoke to more fundamental trends in innovation and biotech industry, which are affiliated with the field. This included the convergence of the scientific bases of biology and chemistry, the need for monitoring of such convergence and co-operation between the BTWC and CWC, the need to monitor commercialisation trends, the need for a survey on the range of chemicals being produced today using biologically-mediated processes, as well as the need to examine the technical feasibility of the chemical synthesis of biological compounds.[84] Three further meetings of the TWG were to follow, with the final meeting taking place in November 2013, and in each case findings were presented to the SAB. In addition, this process also contributed to the production of a substantial report, adopted by the SAB in June 2014.

It is interesting to note that the framing of synthetic biology within the June 2014 SAB report is very similar to how the field has been discussed in papers produced by the Implementation Support Unit from 2006 onwards, which draws on the predominant engineering narrative of the field. This is in the sense that it focuses on the central role of engineering principles (such as modularisation) and emphasises the centrality of metabolic engineering which the report defines as:

> '*science that combines systematic analysis of metabolic and other pathways with molecular biological techniques to improve cellular properties by designing and implementing rational genetic modifications.'*[85]

There is reference, for example, to the aim of modularisation. The report states the advantage of the approach adopted within this field is that:

> '*intensive and often repetitive lab work required in conventional laboratory genetic engineering and molecular biology techniques can often be significantly reduced.'*[86]

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82 Scientific Advisory Board, 'Report of the Third Session of the Scientific Advisory Board' (OPCW, April 2000), 6, http://www.opcw.org/index.php?eID=dam_frontend_push&docID=14877.

83 Scientific Advisory Board, 'Report of the Seventeenth Session of the Scientific Advisory Board' (OPCW, November 2011), 29 at 10.6, http://www.opcw.org/index.php?eID=dam_frontend_push&docID=15239.

84 Ibid., 29.

85 Scientific Advisory Board, 'Convergence of Chemistry and Biology: Report of the Scientific Advisory Board's Temporary Working Group' (The Hague: OPCW, 27 June 2014), 35, http://www.opcw.org/index.php?eID=dam_frontend_push&docID=17438.

It is worth mentioning, that such a framing of synthetic biology, while reflecting some of the most prominent research in the field, does not account for all research that is conducted under the label of 'synthetic biology'.

The report differs from early reviews of the field of synthetic biology in a BTWC context by placing greater emphasis on the growing role of synthetic biology in several sectors of the chemical industry. While to some extent this reflects the fact that understandings of the field and its goals are changing over time, it also reflects different pre-occupations within the OPCW. As is stated in the report of the Science Advisory Board, 'th*e main issue of concern is whether technology could be misused to synthesise toxins, other toxic chemicals or their precursors, in quantities that could pose a threat to the convention'*[87]. This is reflected in the key directives on monitoring developments in fields such as synthetic biology in relation to biological and biological meditated production, the scope of chemicals being studied and produced, rational enzyme design, and the feasibility of using advances in fields of cutting-edge science and technology in the production of toxins. It is worth noting at this point that while this this work is of potential relevance to the scope of the work of the BTWC, it does not encompass all of the concerns which have been expressed in the BTWC forum, including for example concerns about the role of synthetic biology in the manipulation of pathogens.

In saying this, it is also apparent that fields such as synthetic biology may increasingly be understood to necessitate closer working relationships in some areas of implementation. For example the recent recommendations of the CWC SAB report suggests, for us, a need for CWC national authorities (and where they exist BTWC national focal points), to examine the extent to which the convergent nature of fields such as synthetic biology is, or should be, motivating greater institutional collaboration between the fields of biological and chemical risk management at local and national level. It is apparent for example, that large multi-disciplinary synthetic biology research projects, may already be raising new safety and security challenges at local level for institutions which have traditionally been more discipline specific, including the requirement to provide biosafety training to newcomers to biology.

Discussion and Recommendations

The field of synthetic biology has been discussed in the context of the BTWC treaty for more than a decade. However there appears to be no real push for technical consensus on the implications of developments in this field for the convention. This situation is not specific to synthetic biology, and is underpinned by more fundamental short-comings which have come to characterise S&T reviews

86 Ibid., 12.

87 Ibid., 11.

in the BTWC in recent years. Such a situation can be contrasted to the CWC, where synthetic biology has primarily been characterised as a new and improved means for biologically mediated synthesis, which could be misused in the development of existing controlled toxins, or in the development of new toxins.

The differences in discussion over synthetic biology between the CWC and the BTWC reflect the differences in institutional handle and assimilate scientific advice. In the case of the BTWC, the diplomatic community of practice, highly intelligent as it is, is not constituted of biologists or those with expertise and experience within the life science, as Johnson has stated:

> *As ambassadors and their staff are subject to rotation every 3–5 years, and most foreign ministers work on the principle of diplomats as non-specialists, the likelihood of a significant proportion of ineffective representatives being engaged in the multilateral forum is high.*

With only a small number of delegations including scientific advisers, it is perhaps understandable that more nuanced understanding of complexity and potential and specific significance fields such as synthetic biology become lost. This is true for example, when thinking about the potential role of synthetic biology techniques and practises in the development of biological WMD's, and in particular how diplomats and policy makers use framings of biotechnology in order to identify key concerns. Such a situation not only risks negatively stigmatizing certain areas of scientific research, but also risks undermining confidence in ability of regime to help avoid the type of surprises which are driven by innovation, as well its ability to adapt to a post-arms control environment. This then seems a very questionable situation to be in, where even basic steps towards technical assessment are not being agreed, which could help facilitate the identification of the most pressing concerns for the regime, including those driven by advances in S&T.

It is apparent then, that there is a need for a more coherent approach to technology assessment and horizon scanning at the international level. This leads us to make the following recommendations:

> *Recommendation 1: It is uncertain which process States Parties will decide upon for reviewing advances in S&T at the next BTWC review conference. However, it is apparent that there is a need for states to support processes which examine the security implications of fundamental trends which the field of synthetic biology has come to symbolise. This includes, but is not limited to: automation, digitization, de-skilling and rapid commercialisation. It is essential that such processes are linked to action; in terms of norm and capacity building as well as decision making.*

> *Recommendation 2: In addition to reviewing the most recent scientific, technological and industrial developments in the context of the BTWC and CWC, there is a need to*

explore the value of the international community working together to consider, develop, and share information on approaches to technology horizon scanning and assessment as well as anticipatory governance. Such discussions could draw upon a wide range of institutional experiences in reviewing existing and foreseen security concerns associated with cutting-edge fields of innovation at local, national and international level. A good first step would be the convening of an international meeting which focused on these issues and brought together relevant practitioners, national level policy shapers and other stakeholders. Goals of such a meeting could include the identification and comparison of national styles of governance, as well as the identification of basic principles of good governance at local, national and international level. The field of synthetic biology may provide an accessible case study in this regard.