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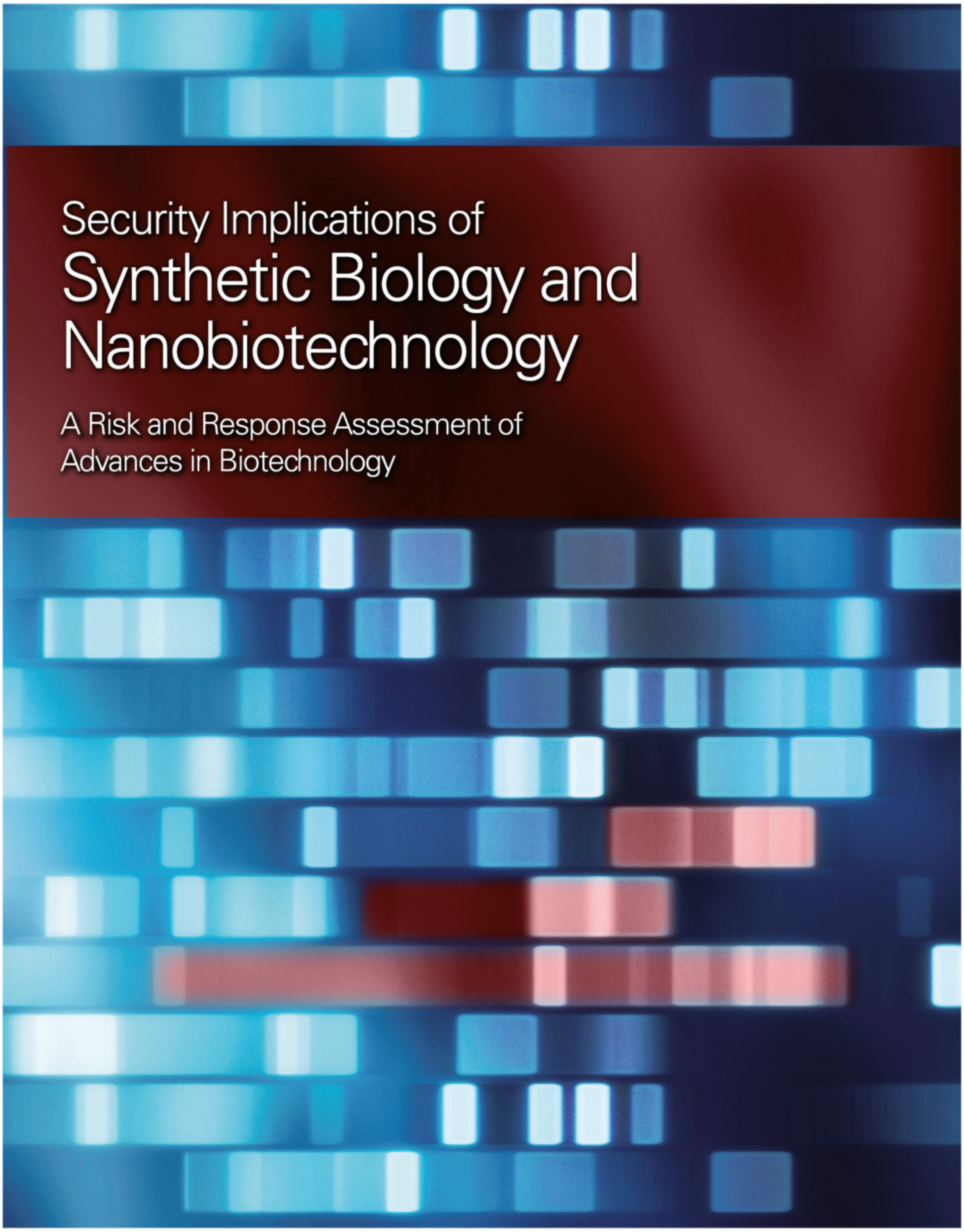

Security Implications of

Synthetic Biology and Nanobiotechnology

A Risk and Response Assessment of Advances in Biotechnology

2012

In cooperation with the
European Commission

This is a shortened public version of the original report
(Part II Section A [pp.12–31] and Part II Section C [pp.36–55] omitted).

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Foreword

By Dr. Jonathan Lucas,
Director, United Nations Interregional Crime and Justice research Institute

The field of biotechnology is in the vanguard of technological trends, which could transform the way we live. The beneficial uses of synthetic biology and nanobiotechnology in medicine, agriculture, renewable energy, nutrition and environmental protection are extensive and real. However, these technologies also bring about safety and security risks as, unfortunately, they can be used by criminals and terrorists.

The United Nations Interregional Crime and Justice Research Institute (UNICRI), an independent UN entity and partner in the UN Counter-Terrorism Implementation Task Force (CTITF), is an innovative contributor to the broad fight against terrorism and gives particular attention to the monitoring of emerging risks in related areas.

The present report documents the results of a pioneering qualitative risk assessment study carried out by UNICRI on the biosecurity implications of developments in synthetic biology and nanobiotechnology. The work has been generously supported by the European Commission. The purpose of the report is to inform and facilitate international discussion and action on the issues at hand. The work is in line with the United Nations Global Counter-Terrorism Strategy, which stresses the importance of ensuring that advances in biotechnology are solely used for the public good.

The project brought together leading international experts from the scientific community, civil society and governments for consultation and debate. The result is a synthesized international and multidisciplinary expert view. It represents a fundamental step towards promoting safe and secure progress in biotechnology. It offers innovative policy options in order to minimize the potential for misuse.

The report highlights the growing need for the international community to work together, with real solidarity, on the biosecurity threats arising from the area of biotechnology – synthetic biology and nanobiotechnology in particular. Innovative strategies must be developed and decisive action taken which ensures that security and ethical issues are taken into consideration in scientific developments. Most importantly, the measures we take must be active rather than reactive. Of course, regulating a field so mutable is not an easy task and we must be dynamic in facing the threats that advances in biotechnology will inevitably bring. This report acknowledges that top down regulation is not nearly enough to cope with the challenges; it issues a rallying call to the international community of science, politics and industry, and to society in general to foster a culture of shared responsibility.

It is our collective responsibility to ensure that future advances in biotechnology, synthetic biology and nanobiotechnology are used only for the benefit of society.

Jonathan Lucas
Director,
United Nations Interregional Crime and Justice Research Institute

Preface

By Ambassador Paul van den IJssel,
President of the BWC Seventh Review Conference

In 1999 Walter Isaacson wrote in Time magazine “Ring farewell to the century of physics, the one in which we split the atom and turned silicon into computing power. It’s time to ring in the century of biotechnology.”[1] Forecasts for our future suggest that the revolution in biotechnology will bear rich fruit and that over the coming decades we will unlock nature’s full potential to better our lives. Advanced biotechnology should enable us to dramatically improve our health, wealth and environment.

Unfortunately, these same technologies could be misused to cause deliberate harm. Every major breakthrough in science has been applied for malign ends. The life sciences are no exception. The same advances that could bring so many benefits could also enable the development of new and improved biological weapons. International efforts to prevent the weaponization of the life sciences are spearheaded by the Biological Weapons Convention. Under the treaty’s auspices, its 163 States Parties undertake to review relevant advances in science and technology and to take all the necessary measures to prohibit and prevent them being intentionally used to cause harm.

In December 2011, States Parties to the Biological Weapons Convention will gather in Geneva, Switzerland, for the treaty’s Seventh Review Conference. There they will “review the operation of the Convention, with a view to assuring that the purposes of the preamble and the provisions of the Convention […] are being realized.” In other words, we will look backwards at what we have achieved since 2006 and forwards to what we wish to accomplish over the next five years.

The security implications of advances in science and technology will be an important facet of all our deliberations. It will be important both this year and for the future, that we approach this topic in a systematic manner. I believe reviewing advances in science and technology to be a three-stage process. First, it is necessary to identify those advances that are particularly relevant. This requires an in-depth understanding of the current status of a wide range of scientific disciplines, necessitating the close involvement of those that actually

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[1] W. Isaacson. 1999. The Biotech Century. In: Time Magazine, 11 January 1999, http://www.time.com/time/magazine/article/0,9171,989981,00.html#ixzz1FYJnIR5m.

practice the science. Second, it is important to examine the implications of the advances identified. This will require an unusual skill set - familiarity with both the science and security issues. It will probably need to draw heavily on national technical expertise. Third, members of the international community will need space to consider if any action, either individually or collectively, is needed to address the implications of these advances.

This report and the project on which it was based are vibrant examples of how we might approach the first two stages of this process. The project was able to draw upon reviews, publications and expert contributions from a broad range of technical specialists to make sense of highly technical areas such as synthetic biology and nanobiotechnology. It also brought together a panel of technical specialists well versed in the security implications of science and technology. The result draws upon these resources to provide a useful overview of the risks derived from, and possible policy responses to, some of the fastest moving and potentially revolutionary areas of modern science. Such works provide an important resource, which the international policy making community, including the Biological Weapons Convention, should draw upon to the fullest extent possible.

I am certain that this report will make a valuable contribution to the work of the Seventh Review Conference and that similar efforts in the future would help us to ensure that the biological sciences are used safely, securely and solely for our benefit.

Paul van den IJssel
Ambassador of the Netherlands to the Conference on Disarmament
President of the BWC Seventh Review Conference

Acknowledgments

This project was made possible through the generous financial support of the European Commission (DG EuropeAid) within the framework of the Instrument for Stability (IfS). The research was conducted by the United Nations Interregional Crime and Justice Research Institute (UNICRI).

Special words of thanks are due to Sergio Bonin for his hard work in supervising the project and preparing the report. Without his efforts this endeavor would not have been successful.

Special gratitude goes to Piers D. Millett, Margaret E. Kosal, R. Alexander Hamilton, and Alexey V. Feofanov for their invaluable scientific support and contributions.

Special words of thanks must also go to Philippe Servais from DG EuropeAid. Also, the efforts of Francesco Marelli, Béatrice Mbayo, Sara Fantoni, Marian de Bruijn, and other UNICRI colleagues need a special mention.

UNICRI and the European Commission are very grateful for the support of the Bioweapons Convention (BWC) Implementation Support Unit (ISU), the Russian Research Center “Kurchatov Institute”, and the Center for Security Studies (CSS) at ETH Zurich.

Sincere thanks go also to Christopher Findlay at the CSS for language editing and proofreading.

Last but not least, UNICRI and the European Commission would like to express their appreciation and gratitude to all the experts, mentioned in Annex to this report, who participated in the workshops in Turin, Italy (March 2010) and in Geneva, Switzerland (June 2010) and provided the main source of information for this report. We are also very grateful to the countries, government agencies, international organizations, and other private and public institutions that participated in the project.

Executive Summary

Bio- and nanotechnology are among the most powerful emerging technologies today. With the dawn and rapid progress of synthetic biology and nanobiotechnology, it is becoming increasingly possible to bioengineer microorganisms, biomolecular components and devices, as well as biotechnical hybrids that perform desired functions. All of these applications can be expected to yield great benefits for human health, environmental protection, and renewable energy sources. The aim behind advances in synthetic biology and nanobiotechnology is both ambitious and controversial: the transformation of biology from a natural science into an applied engineering discipline. Many observers believe that these intertwining technologies herald the next technology revolution.

As with every new technology, however, predictable and unforeseeable risks for society are created, ranging from unintended consequences that are harmful for human health and the environment (biosafety) to the deliberate misuse to cause harm (biosecurity).

The Project

UNICRI's project, in cooperation with the European Commission (EC), focused on the present and future (bio-) security implications of advances in synthetic biology and nanobiotechnology. The project aimed to scan the horizon for developments in the technology fields of synthetic biology and nanobiotechnology that may – depending on their current or future ease of use and access – place potentially dangerous capabilities at the disposal of groups or individuals that are bent on causing harm to society.

This report is the result of two expert workshops held in Turin, Italy and Geneva, Switzerland in March and June 2010. With the broad involvement of bioscience and security experts, a qualitative risk assessment of the potential for malevolent applications of synthetic and nanobiotechnology was undertaken, and a range of promising mitigation measures were debated.

Technology Risks

In the course of the project, experts were able to identify a number of potential avenues for technology misuse, at varying degrees of likelihood and difficulty, that are either enabled or facilitated by technological advances in synthetic biology and nanobiotechnology. Some of these advances pave the way for entirely new possibilities, while others merely provide alternative (and perhaps easier) development pathways for goals that are already achievable using alternative technology options.

In the short term, it is highly unlikely that non-state actors would or could pursue one of these technology paths over easier means of acquiring and employing bioweapons or alternative (conventional) attack options. While that may be possible in specific cases in the medium term as the technologies mature, the potential and capabilities for misuse are likely negligible, and a myriad of beneficial applications can be expected to emerge. While most of the tools and techniques are not within reach of small groups in the short to medium term, some of them are certainly within the capabilities of large organizations or states, should they choose to embark on that path. If the potential of synthetic biology (and of nanobiotechnology, to a certain extent) to make biotechnology more reliable, easier, cheaper, and faster is realized, there could be a significant risk of hostile applications in the longer term by both state and non-state actors.

The dual-use problem in synthetic biology and nanobiotechnology, as in biotechnology in general, is virtually universal: Almost every potential security risk discussed as part of this project can be derived from completely legitimate research endeavors and developments. The nature of advances in bio- and nanotechnology, as well as the consequences of the ability to engineer bio-weapons as desired, could challenge current arms control norms and instruments, in particular the Biological Weapons Convention (BWC).

Synthetic Biology Risks

Should synthetic biology evolve into a full biological engineering discipline in the medium to long term, it could prompt a qualitative shift in capacity compared to standard recombinant DNA approaches. Of particular note would be the dramatic increase in the number of potential users, significant improvements in the reliability of biology-based technology, a substantive reduction in the time taken to translate science into application, as well as distinctly lower resource requirements.

In the short to medium term, synthetic biology is unlikely to create new risks or threats, but it could enable more actors to go down this path. In the long term, the risk or threat posed by a malign actor with access to a full-fledged biological engineering capacity would be quite different from that which we face today. When experts considered whether it was feasible for non-state actors to develop a synthetic biology-based approach to acquire or use biological weapons, it was argued that such a scenario was technically possible, but very difficult and highly unlikely. There was a strong feeling among the experts that alternative acquisition routes or weapons systems would remain prevalent for the foreseeable future. If synthetic biology succeeds in lowering the barriers to biological technology sufficiently, advanced biotechnological capabilities might become available to a much wider range of actors, and the vast field of biology would become more accessible to “non-experts”.

As an enabling tool, and in addition to assisting in many beneficial applications, synthetic biology could in the long term facilitate the work of those attempting to acquire and use biological weapons. More dangerous and controllable pathogens could be engineered that lead to novel possibilities in designing bioweapons. Advances in modeling could enable improvements in weapons design. Metabolic engineering might confer new qualities and attributes upon agents and offer options for new types of weapons. The ability to manipulate agents systematically for specific ends could assist in overcoming current hurdles to an effective attack, such as detection modalities, challenges to effective release, and environmental instability. This could have the negative effect of making bioweapons cheaper and easier to acquire, eventually making their use more likely; more reliable and controllable, making them more desirable; and more effective, increasing their potential impact.

However, the ability to respond to an attack is also a function of risk. Synthetic biology will offer just as many, if not more, opportunities to develop prophylactics and therapeutics as it will with regard to weapons. Experts felt that it was too early to establish the net effect of synthetic biology with regard to compounding as well as mitigating biological risks and threats.

Nanobiotechnology Risks

Nanobiotechnology offers a multitude of potential risk scenarios of varying likelihood and potential consequence. Like synthetic biology, nanobiotechnology currently does not constitute an entirely new dimension to the bioterrorism threat; instead, it was largely viewed as a means to create more potent, nano-enabled bioweapons. Because nanobiotechnology is such a diverse field comprising a range of materials and methods, gauging the risk and threat precisely is an extremely complicated undertaking. There is no single entity or technique that can be singled out as the sole or even major area of concern. This makes devising and implementing domestic and international regulations significantly more complicated.

Nanobiotechnology might afford methodologies, ranging from the simple to the highly complex, that would make it possible to use agents previously not considered as bioweapons by attaching them to nanoparticles. Nanotechnology was also recognized as a potential means of facilitating weaponization – for example, by enhancing the environmental stability of biological agents in such a way that their reliability or environmental robustness is increased, potentially making such agents more attractive in the medium to long term.

It is currently harder to develop a nanobiotechnology capability than achieve a similar capability in the field of synthetic biology. Due to the divergent and heterogeneous nature of nanotechnology, the barriers of entry are different, and in many (but not all) cases, higher. For the foreseeable future, the technology is primarily within reach of potential state programs, or possibly rogue scientists working within such programs, also because terrorists are much more likely to employ cruder bioweapons than to embark on this complicated technology path. In the short term, it is highly unlikely that non-state actors would choose the nanotechnology path over easier means of acquiring and employing bioweapons, but it might occur in specific cases in the medium term. There could be a significant risk of nefarious applications in the longer term, as the underlying technologies mature.

Response Options

The nature of progress in biotechnology will, if it has not already, likely negate the ability to control the technology with traditional means. Expertise, materials, and equipment are already available to varying degrees around the globe and, accordingly, the proliferation of knowledge and expertise – although not necessarily weapons-related – has already taken place. It is very likely that relevant knowledge, equipment, and personnel will spread further to new geographical locations and societal sectors. Synthetic biology and nanobiotechnology might constitute initial steps towards a qualitative and quantitative paradigm shift in biotechnology and may revolutionize the manner in, and scale at, which biological work will be conducted in the future.

While international arms control agreements and norms will continue to play an important role, the increasing penetration of society by biotechnology, including the emergence of a subculture outside traditional confines, clearly warrants a broader policy response to tackle the wider societal aspects and impacts. Instead of only trying to control and deny access through international arms control measures, experts emphasized that the focus of securing biology should be shifted towards developing a shared responsibility between policy-makers, scientists, and technologists, as well as society at large.

To tackle the potential negative long-term implications of progress in biotechnology, while ensuring that beneficial research is not impeded, the majority of experts engaged in this assessment suggested that the international community should, in addition to strengthening established norms and taboos against bioweapons development and use, move beyond attempts to regulate and control these developments towards managing them more comprehensively by complementing traditional approaches with innovative initiatives and concepts.

The focus should be shifted towards creating a shared responsibility of politics, industry, science, and society to reinforce a culture of safety and security in biotechnology and minimize the risks by engaging relevant communities and empowering various actors to detect and report abuses. This requires fostering a worldwide culture of awareness and responsibility in biotechnology as well as building a network of relevant public and private actors, top-down and bottom-up measures, initiatives and checks on the national and international levels covering all relevant activities and linking all levels of society in a comprehensive and systematic way.

Part 1

Introduction

Bio- and nanotechnology are among the most powerful emerging technologies today. With the emergence and rapid advance of synthetic biology and nanobiotechnology, it is becoming increasingly feasible to bioengineer microorganisms, biomolecular components and devices as well as bio-technical hybrids that perform specified functions. These technologies can be expected to bring great benefits for human health, environmental protection, and renewable energy sources. The aim behind advances in synthetic biology and nanobiotechnology is both ambitious and controversial: the transformation of biology from a natural science into an applied engineering discipline. Many observers believe that these intertwining technologies herald the next technology revolution, offering an early indication of potential future developments, and are poised to become the transformative innovations of the 21st century.

Largely due to the development and ongoing advancement of automated machines that can sequence (i.e., “read”) and synthesize (i.e., “write”) genetic material (DNA), synthetic biology promises to enable the modification of microorganisms for the production of pharmaceuticals, the destruction of cancer cells, the remediation of polluted sites, and the generation of biofuels. Since biological entities are organized on the nanoscale, nanobiotechnology offers the insights and tools needed to transform biosystems, while taking inspiration and components from biological materials and principles to create new devices and systems. It is expected to provide new and improved systems for medical diagnostics, targeted drug delivery, as well as enhanced therapeutics and pharmaceuticals.

As with every new technology, however, these developments are attended by predictable and unforeseeable risks for society, ranging from unintended harmful consequences for human health and the environment (biosafety) to the deliberate misuse to cause harm (biosecurity). It might become possible in the future to synthesize and/or alter the properties of many pathogens whose DNA sequence is known or to engineer microorganisms not found in nature. Nanobiotechnology might provide the tools to facilitate the weaponization of biological agents and increase their effectiveness. These developments might enable the design of new and more potent bioweapons.

However, the disciplines are still in their infancy, and the majority of work that is being done is on the level of basic research. The technical hurdles are considerable, and the required know-how is still concentrated on a relatively small scientific community. With the current pace of developments, though, this could change within the coming decades, which requires that the potential dangers be addressed early on, while allowing for the unhindered development of beneficial applications.

The Project Report: Scope, Aims, and Methodology

UNICRI's project, in cooperation with the European Commission (EC), focuses on present and future (bio-) security implications of advances in synthetic biology and nanobiotechnology. It examines the vast dual-use potential of these technology fields – i.e., the fact that many beneficial applications could be misused for hostile purposes – with a focus on their suitability to enable the development of new or enhanced biological agents and weapons, primarily for criminal or terrorist purposes. The project aimed to scan the horizon for developments in the technology fields of synthetic biology and nanobiotechnology that – dependent on their current or future ease of use and access – may cause potentially dangerous capabilities to be placed at the disposal of groups or individuals that intentionally want to cause harm to society.

With the broad involvement of bioscience and security experts, a qualitative risk assessment of the potential for malevolent applications of synthetic biology and nanobiotechnology was undertaken, and a range of promising mitigation measures were debated. In the course of these activities, a series of potential emerging biological threats and areas requiring further attention were identified.

This report is the result of two expert workshops held in Turin, Italy and Geneva, Switzerland in March and June 2010 under the Chatham House Rule. Throughout the project, a topically broad group of around 35 experts and stakeholders from national government agencies, international organizations, academia/research, the security community, and the private sector has been engaged.

The first workshop examined potential (bio-) security risks associated with advances in synthetic biology and nanobiotechnology and their implications. As this is a domain of cutting-edge high technology, the project necessarily had to look into the future. It was felt that the "traditional" method of assessing the likelihood of a risk materializing, together with its potential impact, was difficult to perform and not conducive to real foresight, due to the many uncertainties and unknowns associated with the two technology fields at this stage of development.

Instead, the project followed a scenario-based approach. Technology risk scenarios – i.e., what kind of technical opportunities for misuse could be enabled by the two emerging technology fields – were developed and compiled by UNICRI together with certain experts and/or taken from existing literature before the risk workshop. The resulting working documentation of technological possibilities and risks ("scenarios") formed the basis for the discussion and assessment of the individual technical issues, based on a scientifically grounded technological outlook.

Apart from the individual, more technical issues, experts were also asked to consider a number of particular aspects, such as the technological feasibility over time; the level of difficulty regarding required capabilities (i.e., skills, knowledge, resources, equipment, etc.); and the practicability from a perpetrator's point of view. In addition, some specific security aspects such as bioweapons proliferation and the nature of enabled risks were examined.

Project participants were asked to think in the following timeframes:

- In the short term: within the next five years;
- In the medium term: between five and 20 years; and
- In the long term: more than 20 years.

The second project workshop dealt with possible governance options and response measures to address the challenges and risks associated with synthetic biology and nanobiotechnology. Here, a less standardized procedure was chosen. Several experts presented their proposals and views on possible response and mitigation measures that are either already in place or could be established in the future to respond to the challenges identified, which were than examined and discussed at the second project meeting. For the purpose of this report, the experts' response assessment and remarks were complemented with information and facts from existing literature and other sources in order to provide the reader with the necessary background knowledge.

It soon became clear that it does not make sense, apart from a few peculiarities, to view in isolation the question of how to address detrimental developments in synthetic biology and nanobiotechnology, but that it has to be examined in the broader context of biotechnology as a whole. The field of nanobiotechnology was mainly considered within this biotechnology context, even though it could also be addressed in the framework of nanotechnology. However, while we touch on that field on several occasions, the focus is on biology, and entering the governance discussion on nanotechnologies is beyond the project's scope. Furthermore, workshop deliberations did not go into details of national regulatory and legislative issues.

Neither the risk assessment nor the response assessment provide a complete picture of potential risks and available mitigation options, but they highlight core areas that were emphasized by our expert panel.

During both workshops, experts also debated the emergence of an amateur biologists' movement on the margins of modern biotechnology outside traditional institutional settings, as well as related safety and security concerns. Even though the vast majority of amateurs do not currently employ any synthetic or nanobiology techniques, the growing community is seen as an expression and early affirmation of many observers' expectations of what, among other developments, synthetic biology most prominently heralds, i.e., a biotechnology revolution that will penetrate deep into society.

An issue that was deliberately avoided from the outset of the project was the development of a definition of synthetic biology and nanobiotechnology, as this could have derailed the project's focus and prevented more productive discussions. Narrow demarcations were felt not to be necessary and expedient for this kind of project and the issues at hand.

Participating experts repeatedly reviewed draft versions of this report.

Structure of the Report

The following sections provide an overview and general introduction to synthetic biology and nanobiotechnology.

Part II contains the individual technical scenarios for misuse pertaining to synthetic biology or nanobiotechnology respectively, which are introduced and discussed based on experts' assessments. For each individual issue, an assessment summary table is provided to offer a quick estimate regarding the technical feasibility and level of difficulty of the individual technological scenarios over time. Following this discussion, general security aspects and implications for each of the two technology fields are examined. The subsequent section briefly considers the potential motivations of several kinds of actors to misuse synthetic biology and nanobiotechnology techniques to cause deliberate harm.

Part III outlines possible governance and response options to tackle some of the challenges. The first section outlines the characteristics of a networked approach of different measures on various intervention levels, as emphasized by participating experts, to address the security implications of progress in biotechnology. This is followed by several more concrete mitigation elements that are important components of such a web of activities. These include: outreach, education, and awareness-raising; codes of conduct and screening frameworks;

international arms control and non-proliferation; and technical response measures enabled by synthetic biology and nanotechnology. Throughout the response part, recommendations are provided for each of the highlighted elements.

The final section provides an introduction to the amateur biologists movement, outlines some of the main concerns commonly associated with it, and discusses options for addressing them.

Synthetic Biology Overview

Although there is no single, agreed upon definition of ‘synthetic biology’, this emerging area of scientific research can be broadly understood as “the deliberate design of biological systems and living organisms using engineering principles”.[2] Having developed as a result of the convergence of scientific knowledge, techniques, and tools, synthetic biology draws on, and shares certain similarities with, other disciplines such as systems biology, genetic engineering, mechanical and electrical engineering, information technology, physics, chemistry, nanotechnologies, and computer modeling, etc. Irrespective of how it is defined and classified, however, the potential of synthetic biology to ‘deskill’ the art of genetic engineering, by way of making the design and construction of living systems easier and more widely accessible, is deemed to pose new opportunities and risks.

Within synthetic biology, several strands of research have been identified as being indicative of the specific approaches employed by ‘synthetic biologists’ today. Broadly speaking, these approaches can be defined as ‘top-down’ or ‘bottom-up’ (or, most often, a combination of the two), where top-down refers to the practice of synthesizing and inserting functional biological components into entire genomes, and bottom-up refers to the practice of synthesizing functional biological components or whole genomes from scratch.[3] More specifically, these approaches can be divided into several categories, including:[4]

- DNA-based device construction, which seeks to design and construct standardized genetic parts from synthetic DNA that can be used to assemble metabolic pathways or ‘genetic circuits’;

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[2] A. Balmer and P. Martin. 2008. Synthetic Biology: Social and Ethical Challenges. Institute for Science and Society, University of Nottingham, p. 3.

[3] Cf. M.A. O’Malley, A. Powell, J.F. Davies and J. Calvert. 2007. Knowledge-making distinctions in synthetic biology. In: BioEssays, 30, pp. 57-65. A. Balmer and P. Martin. 2008. Synthetic Biology: Social and Ethical Challenges. Institute for Science and Society, University of Nottingham.

[4] Adapted from M.A. O’Malley, A. Powell, J.F. Davies and J. Calvert. 2007. Knowledge-making distinctions in synthetic biology. In: BioEssays, 30, pp. 57-65.

- Genome-driven cell engineering, which seeks to synthesize entire genomes, including minimal genomes (or 'chassis') that can be used as versatile platforms to 'run' genetic parts or circuits; and
- Protocell creation, which seeks to construct viable living cells and cellular systems from synthetic DNA, mimicking naturally occurring life.

In each case, rapid productivity gains in DNA sequencing and synthesis, combined with rapid declines of the costs associated with these techniques, have been identified as key drivers in advancing research and development in synthetic biology, as they afford researchers increased capacity to 'read' and 'write' genetic code.[5] Increasingly, sequencing and synthesis activities are outsourced to firms that specialize in gene- or genome-length DNA sequencing and synthesis, allowing researchers to focus on the design and construction phases of their research projects.

Prominent synthetic biology approaches and researchers

In an effort to illustrate further the scope and potential of synthetic biology approaches, it is worth highlighting how several prominent researchers view, and use, synthetic biology.

- Drew Endy and Tom Knight have played an influential role in shaping the modular 'parts-based' approach to the field, calling for efforts to make synthetic biology a true engineering discipline, complete with the necessary tools, techniques, and protocols needed to rationally design and construct novel living systems.[1] Their approach favors the design of standardized modular genetic parts that can be mixed and matched to construct living machines that can perform specific functions. In pursuit of this objective, the Massachusetts Institute of Technology's (MIT) Registry of Standard Biological Parts[2] maintains a growing collection of genetic parts with (more or less) predictable functions, many of which are developed and used by student teams that participate in the annual International Genetically Engineered Machines (iGEM) competition held at MIT.
- The International Genetically Engineered Machines (iGEM) competition[3] is an undergraduate synthetic biology competition that draws young academics from around the world and different disciplines into the field. Student teams compete to design and test a biological system from standard, interchangeable parts and operate it in living cells. In 2010, 130 teams and about 2,000 participants participated in the competition and in the end-of-year iGEM Jamboree.
- The J. Craig Venter Institute (JCVI) has played an equally significant role in shaping the field, pioneering the construction of a minimal or chassis genome, which is intended to serve as a viable platform for the insertion of synthetic genes or circuits that could express any number of useful products from vaccines to bio-fuels.[4] More recently, Venter and colleagues made headlines after they reported the design, synthesis, and assembly of the Mycoplasma mycoides JCVI-syn1.0 genome, which they subsequently transplanted into a recipient cell, creating the first synthetic living cell.[5] This research is pushing the limits of DNA synthesis technology to produce ever-larger genomes, including viral and bacterial genomes, and is also challenging former understandings of natural life. Moreover, JCVI's chassis may further enable the parts-based approach to synthetic biology, providing a simplified platform for

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[5] R. Carlson. 2003. The pace and proliferation of biological technologies. In: Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science, 1(3), pp. 203-214.

the insertion of standardized modular genetic parts and the assembly of genetic circuits.

- George Church, a molecular geneticist at Harvard Medical School, has been, and continues to be, influential both in terms of advancing synthetic biology and in commenting on how it could be misused and governed. On the one hand, Church is recognized for his imaginative, future-oriented approach to synthetic biology and for his work on the Human Genome Project. On the other hand, in a 2005 Nature article, Church suggests "a code of ethics and standards should emerge for biological engineering as it has done for other engineering disciplines."[6] Also in this article, he outlines possible laboratory containment standards, environmental protection measures, and the need for imagining worst-case scenarios, in an effort to protect against the potential risks posed by synthetic biology. In many ways, Church is emblematic of contemporary synthetic biology practitioners, in that he is enthusiastic about the possibilities of the field while also remaining cautious considering how the knowledge, techniques, and tools of synthetic biology could be misused.

1 D. Endy. 2005. Foundations for engineering biology. In: Nature, 438(24), pp. 449-453.
2 http://partsregistry.org/.
3 http://igem.org/.
4 D.G. Gibson et al. 2008. Complete chemical synthesis, assembly, and cloning of Mycoplasma genitalium genome. In: Science, 319(5867), pp. 1215-1220.
5 Cf. D.G. Gibson et al. 2010. Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome. In: Science, 329(5987), pp. 52-56.
6 G. Church. 2005. Let us go forth and safely multiply. In: Nature, 438(7067), p. 423.

In brief, synthetic biology is an emerging area of scientific research that promises to greatly enhance the capacity of scientists (and possibly even hobbyists) to design and engineer new forms of life, including dangerous pathogens. Whether or not synthetic biology will achieve its stated aims and become a true engineering discipline that permits a greater number of people to pursue modern biology remains to be seen. Nonetheless, ambitious plans exist for to making such a potential a reality. Moreover, as the successes of synthetic biology practitioners (see text box) suggest, considerable strides are being made in DNA sequencing and synthesis, including the application of these techniques in the fabrication and assembly of synthetic parts, circuits, genomes, and cells. Such advances suggest an urgent need to take stock of the science and its potential for both beneficial and dangerous applications.

Nanobiotechnology Overview

Technological advances enabled by nanoscience, along with information science and biotechnology, are major drivers in advances in emerging sciences. Nanotechnology, encompassing a broad spectrum of nanoscale science and engineering, can be described as an array of fundamental knowledge and enabling technologies resulting from efforts to understand and control the properties and function of matter at the nanoscale.[6] Nanotechnology is not a specific deter-

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[6] US National Research Council. 2006. A Matter of Size: Triennial Review of the National Nanotechnology Initiative. National Academies Press: Washington, D.C.

minate homogenous entity, but a collection of diverse capabilities and applications, with expectations of synergies among them.

The nanoscale – measured in nanometers, a millionth of a millimeter – can be applied to both natural and man-made objects. For instance, DNA, some cells, molecules, and the length scale of biochemical processes inside cells are measured on this scale. A single water molecule is approximately one-tenth of a nanometer wide; hemoglobin – the globular protein responsible for carrying oxygen from the lungs to the body's tissues – is five nanometers in diameter. At the nanoscale, phenomena are no longer dominated by bulk properties. Biologists, chemists and others routinely deal with these small building blocks.

Nanotechnology and biotechnology enjoy a great deal of overlap in many research laboratories. Nanobiotechnology, as the name suggests, refers to the interface between, and convergence of, nano- and biotechnology. It is a multidisciplinary field of research that is based on an array of technologies contributed by various disciplines such as chemistry, physics, biology, and engineering.

Nanobiotechnology can be broadly described as "a field that applies the nanoscale principles and techniques to understand and transform biosystems (living or non-living) and which uses biological principles and materials to create new devices and systems integrated from the nanoscale."[7] Accordingly, nanobiotechnology basically refers to the application of nanotechnology to the life sciences and may also include the reverse, the application of bio- to nanotechnology (e.g., biomimetics; the application of principles from nature to create new materials, devices and systems)[8] – the latter is sometimes referred to as 'bionanotechnology', although the two terms are often used interchangeably. For the purposes of this project and report, nanobiotechnology was primarily considered in the framework of biotechnology, as the focus is on bioweapons (and not, for instance, on "nanoweapons" mimicking bioweapons).

Among other uses, the current and potential future applications of nanobiotechnology – especially in medicine, but also in agriculture and environmental protection – include:[9]

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7 M.C. Roco. 2003. Nanotechnology: convergence with modern biology and medicine. In: Current Opinion in Biotechnology, 14, p. 337.

8 Cf. Ibid., pp. 337-346. See also Wei Zhou. 2003. Ethics of Nanobiotechnology at the Frontline. In: Computer and High Technology Law Journal, Vol. 19, pp. 481-489.

9 Adapted from O. Shoseyov and I. Levy (eds.). 2008. NanoBioTechnology: Bioinspired devices and materials of the future. Humana Press: Totowa, New Jersey. And, The Royal Society and the Royal Academy of Engineering. 2004. Nanoscience and nanotechnologies: opportunities and uncertainties. RS/RAENG: London.

- Therapies that facilitate the targeted delivery and controlled release of drugs and genes to affected cells, where the impact is most effective and precise, without harming neighboring cells or tissue;
- Targeted cancer therapies that destroy tumor cells with light (lasers) or magnets, which leaves healthy cells intact and drastically reduces side effects;
- Array technologies and biosensors for diagnostics and detection purposes, which offer high sensitivity and quick results while requiring lower amounts of biological samples. So-called "lab-on-a-chip" technologies could be used for the real-time diagnosis/detection and analysis of diseases, cells, and microorganisms, including the detection of pathogens used in a bioterrorist attack; and
- Various other potential applications, such as discovery of new drugs by studying drug-receptor interactions at the molecule level; medical imaging; implants and prosthetics; molecular self-assembly as a fabrication tool; and nanocomputing by engineering biomolecules, such as DNA-based computer circuits.

Convergence of Synthetic Biology and Nanobiotechnology

Synthetic biology and nanobiotechnology are viewed by many as two of the most promising and powerful emerging technologies today. In as much as the two technology trends can be thought of as 'emerging technologies', which are presently pushing the limits of science and technology, these innovative areas of research can also be considered 'converging technologies', since they exist at the intersection of multiple scientific disciplines.

In a 2002 report by the US National Science Foundation, the authors refer to converging technologies as arising from the synergistic combination of:[10]

a) Nanoscience and nanotechnology;
b) Biotechnology and biomedicine, including genetic engineering;
c) Information technology, including advanced computing and communications; and
d) Cognitive science, including cognitive neuroscience.

Taken together, this is often referred to as "NBIC", an acronym for Nanotechnology, Biotechnology, Information technology, and Cognitive science. Convergence, the authors argue, is "based on material unity at the nanoscale and on technology integration from that scale", enabling the production of "trans-

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[10] M.C. Roco and W.S. Bainbridge (eds.). 2002. Converging Technologies for Improving Human Performance: Nanotechnology, Biotechnology, Information Technology and Cognitive Science. US National Science Foundation.

forming tools" that will permit humankind to "understand the natural world, human society, and scientific research as closely coupled complex, hierarchical systems."[11]

As noted above, the field of nanobiotechnology already constitutes the convergence and integration of nanotechnology with biotechnology. Moreover, there have also been explicit calls for a specific combination of nanobiotechnology with synthetic biology in order to harvest the full potential of the two technology fields, as they offer the prospect of synergies that might achieve more than either technology alone.[12] Both disciplines are located at the intersection of biology and technology, apply an engineering approach to biology, and challenge the distinction between living and non-living systems. These two innovations already overlap to a certain degree, not only with regard to some of their technical aspects, but also concerning their potential social and ethical impacts.[13] Their partial convergence is expected to accelerate, which could unfold a significant transforming potential in the coming decades.

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[11] Ibid., p. IX.

[12] See, for instance, the Ilulissat Statement – Synthesizing the Future: A vision for the convergence of synthetic biology and nanotechnology. Kavli Futures Symposium Report, June 2007, Ilulissat, Greenland.

[13] Cf. A. Deplazes. 2008. Nanobiotechnology and Synthetic Biology: Two Forms of Overlap Between Biology and Technology - A Comparison of Scientific, Social, Ethical and Philosophical Aspects of the Two Disciplines. In: J.S. Ach and C. Weidemann (eds.). 2008. Size Matters: Ethical, Legal and Social Aspects of Nanobiotechnology and Nano-Medicine. Berlin-Hamburg-Munster, pp. 51-74.

Part 2

Risk Scenarios and Potential Security Implications of Progress in Synthetic Biology and Nanobiotechnology

In the following, the current state of, and potential future developments in, synthetic biology and nanobiotechnology regarding the potential for misuse of relevant individual techniques to enable the creation of new or enhanced biological agents and weapons are discussed and assessed. The individual options were partly compiled before the risk workshop and formed the basis for deliberations within the meeting. Each of the following subsections contains an 'assessment summary table' intended to provide a quick estimate regarding the technical feasibility and level of difficulty of the individual technological scenarios over time.

Sections A and B examine the potential for misuse of individual synthetic biology approaches and the wider security implications of the field respectively. Sections C and D correspondingly assess nanobiotechnology approaches and implications. In section E, incentives of different kinds of perpetrators to misuse synthetic biology or nanobiotechnology techniques are discussed.

Project participants were asked to think in the following timeframes:

- In the short term: within the next five years;
- In the medium term: between five and 20 years; and
- In the long term: more than 20 years.

As for the assessment summary tables on each individual issue, the level of difficulty was codified as follows:

- Easy: "Student with basic knowledge and an improvised desktop laboratory setting"; e.g., small terrorist group, rogue individual
- Moderately difficult: "PhD-level scientist with some experience, money (~30'000$), and access to adequate equipment"; e.g., terrorist group, rogue individual

- Difficult: “Experienced scientist (or group of) with expertise, money (∼100’000$), and laboratory access”; e.g., terrorist organization, rogue scientist, organized crime
- Very difficult: “Large organization with sufficient funds, time, resources, and long-term goals”; e.g., large organizations, states, transnational actors

A. Synthetic Biology Scenarios: Technological Possibilities and Risks

This is a shortened public version of the original report
(Part II Section A [pp.12–31] and Part II Section C [pp.36–55] omitted).

B. Security Implications of Synthetic Biology

Workshop participants generally noted that if synthetic biology should evolve into a full biological engineering discipline in the medium to long term, it could prompt a qualitative shift in capacity compared to standard recombinant DNA approaches. Of particular note would be the dramatic increase in the number of potential users, significant improvements in the reliability of biological-based technology, a substantive reduction in the time taken to translate science into application, as well as distinctly lower resource requirements.

Experts also stressed the myriad positive applications that would stem from biological engineering.[36] It was felt that such applications would be too important for continued human development to impede. It was also recognized that it would prove impossible to entirely remove the risk of synthetic biology enabling the creation and use of biological weapons. Experts concluded that dealing with the negative potential of synthetic biology would be a process of managing and not removing risk.

Actors' Capabilities and Feasibility

Experts felt that in the medium term, synthetic biology as an enabling technology could streamline the application of biological knowledge and lead to a range of new applications. Those applications themselves would not be dependent upon synthetic biology, but would likely happen sooner and more cheaply and be more reliable because of it. Experts noted that in the short to medium term, synthetic biology is unlikely to create new risks or threats, but could enable

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[36] Cf. also Institute for Prospective Technological Studies. 2007. Consequences, Opportunities and Challenges of Modern Biotechnology for Europe – The Bio4EU Study. European Commission, Joint Research Centre, Seville.

more actors to go down this path.

In the long term, the risk or threat posed by an malign actor with access to a fully realized biological engineering capacity would be quite different from that which we face today. Experts noted that continuing engagement on security issues by the synthetic biology and wider biotechnology community would help counteract the potential impact of more people having access to biological technology.

When experts considered whether it was feasible for non-state actors to develop a synthetic biology-based approach to acquire or use biological weapons, it was argued that such a scenario was technically possible, but very difficult and highly unlikely. There was a strong feeling among the experts that alternative acquisition routes or weapons systems would remain prevalent for the foreseeable future. Experts did note, however, that if synthetic biology succeeded in lowering the barriers to biological technology sufficiently, advanced biotechnological capabilities might become available to a much wider range of actors, and the vast field of biology would become more accessible to “non-experts”.

Nonetheless, the tools, techniques, and approaches that currently lie outside the grasp of small groups are well within the capabilities of states and large organizations with the necessary resources. If such actors should choose to invest sufficient time, resources, and money in the short to medium term, they would likely be in a position to use synthetic biology to facilitate their acquisition or use of biological weapons. Over the longer term, synthetic biology could significantly lower the hurdles such actors face. Experts noted that some states have motives for looking into these issues and that some of the scenarios discussed highlighted developments that might make biological weapons more desirable. The potential to engineer biological systems would also offer opportunities for new types of biological weapons.

By reducing the time to go from concept to application, synthetic biology has the potential to complicate interdiction efforts. The boundaries between defensive and offensive research and development may also be further blurred by a generic capacity to model, design, create, and optimize biological technology, and the exact motives are hard to pinpoint. Traditionally, there are also connections between state weapons programs and terrorist capabilities, and the possibility of non-state actors acquiring weapons from a state cannot be ruled out. In this context, it is important to note that any application of synthetic biology for acquiring or using biological weapons would be covered by the terms of the Biological Weapons Convention (BWC) – many would fall under the Chemical Weapons Convention (CWC) as well – and therefore be inconsistent with international law (see also response section below).

Nature and Dimension of Risks

Discussions across several of the above scenarios highlighted the future potential of synthetic biology. Experts repeatedly noted that current research will likely mature in the short to medium term, and the underlying technologies will likely become more accessible and commonplace. As a result, experts felt that the application of synthetic biology for nefarious purposes was unlikely in the short term, but possible in specific cases in the medium term. As the stated aim of synthetic biology is to make biological technology more reliable, easier, cheaper, and faster, there could be a significant risk of hostile application in the longer term if its potential should be realized.

Experts felt that for the foreseeable future, synthetic biology was unlikely to replace acquisition from nature or diversion as the most likely route for the acquisition of a traditional agent. They noted that this might change in the future as DNA synthesis capabilities improve, biosecurity becomes more robust, and natural diseases become less prevalent.

Experts felt that as an enabling tool, synthetic biology, in addition to assisting in many beneficial applications, would in the long term likely facilitate the work of those attempting to acquire and use biological weapons. More dangerous and controllable pathogens could be engineered that lead to novel possibilities in designing bioweapons. Advances in modeling could enable improvements in weapons design. Metabolic engineering might confer new qualities and attributes upon agents and offer options for new types of weapons. The ability to manipulate agents systematically for specific ends could assist in overcoming current hurdles to an effective attack, such as detection modalities, effective release challenges, and environmental instability. This could have the negative effect of making bioweapons cheaper and easier to acquire, making their use eventually more likely; more reliable and controllable, making them more desirable; and more effective, increasing their potential impact.

The most immediate near-term concern associated with synthetic biology in the coming decades might be the design of metabolic pathways in bacteria to produce toxic agents, according to the majority of workshop participants. In the longer term, the potential for synthetic biology tools to make biological weapons more desirable, easier to acquire, and potentially more effective makes the technology something of a “game-changer”. Selective bioweapons would remove many of the existing hurdles for military use. Military research and development could increase and lead to bioweapons that allow targeted use with a much lower risk of affecting one’s own troops or population. The suspicion that potential adversaries might go down such a path could provide strong motives in some countries to follow suit, thus endangering the BWC.

Experts also noted that the ability to respond to an attack is also a function of risk. Synthetic biology will offer just as much, if not more, opportunities to develop prophylactics and therapeutics as it will with regard to weapons (see also response section below). Experts felt that it was premature to be able to establish the net effect of synthetic biology with regard to compounding as well as mitigating biological risks and threats. They felt that synthetic biology will ultimately enable a raft of measures to reduce the threat posed by biological weapons.

Discussions also covered threat perception. Experts felt that the public perceptions of the risks and threats posed by synthetic biology might be more likely to have a detrimental effect on its development than the threats and risks themselves. It was felt that a large-scale safety incident involving synthetic biology could prompt a public backlash that would press policy-makers to react more strongly than they would otherwise. The impact of such events can be influenced by the way the community identifies and addresses risks and threats before they happen and reacts to them if they do. A comprehensive risk management framework that addresses both safety and security issues would be important for tackling these concerns.

Dual-Use Potential and Implications for Bioweapons Proliferation

The advent of synthetic biology coincides with significant investment in biotechnology around the world. Many countries are investing heavily in infrastructure, and research is increasingly global in nature. Biological knowledge, tools, and resources are spreading around the world. Some observers are concerned this may facilitate proliferation, since there is little to stop these resources from being diverted to make weapons. As a result, there is an increasing focus on regulating the flow of certain equipment and materials. Because synthetic biology tools compound the dual-use nature of standard technology and pave the way for conceiving of biology in increasingly abstract terms, they may pose additional challenges to existing control regimes.

In the view of many experts, the nature of biotechnology and progress in this field will likely negate our ability to control the technology to a large extent – it will spread too far, too quickly, and to too many actors for top-down regulation to be able to keep up. Controlling biotechnology with the same tools as used to control nuclear weapons technology would also seem counter-intuitive. Whilst nuclear weapons development requires highly specialized expertise and specific types of equipment, biological weapons could be made using generic dual-use equipment and approaches that require much less expertise.

As opposed to nuclear technology, where materials, equipment, and knowledge are limited in scope, very expensive, and easily detectable, modern biotechnology is increasingly prolific, cheap, and dual-use in nature. Experts felt that many of the approaches used for beneficial purposes could be quite easily adapted for malevolent use. As the biotechnology revolution and synthetic biology continue to expand, it is likely that relevant knowledge, equipment, and personnel will spread to new geographical locations and societal sectors. Accordingly, advances in biotechnology will likely complicate efforts to stop proliferation.

As the skill sets are shared more widely and as synthetic biology reduces the reliance on tacit knowledge – a key limiting factor of proliferation in biotechnology – additional hurdles to the acquisition and use of biology weapons will be eroded. Experts concluded that in the longer term, this might be the area where synthetic biology has the greatest impact on the potential for biology to be used as a weapon.

C. Nanobiotechnology Scenarios: Technological Possibilities and Risks

This is a shortened public version of the original report
(Part II Section A [pp.12–31] and Part II Section C [pp.36–55] omitted).

D. Security Implications of Nanobiotechnology

Actors' Capabilities and Feasibility

Experts concluded that it is currently harder to develop a nanobiotechnology capability compared to synthetic biology. Due to the divergent and heterogeneous nature of nanotechnology, the barriers of entry are different and in many (but not all) cases, higher. The required skill sets are more diverse and accordingly less likely to be concentrated in individual persons or fields. However, experts also noted that one would not necessarily need expertise in all areas for nefarious activity.

While it is possible to order nanoparticles such as capsules or carriers from commercial suppliers, the ordering procedure is not as straightforward as ordering synthetic DNA, and the possibilities for obtaining specialized parts for a particular application require technical competence and familiarity. Raw materials and equipment are available, but applied knowledge and expertise, especially for specialized applications and their implementation, are much more diversified across numerous fields and applications compared to synthetic biology.

If particles are needed for very particular purposes, they might need to be self-made. However, capsules or carriers for various applications have already been developed, e.g., in industry, and it is possible, although not probable, that they could be obtained and conceivably filled with a toxic agent. According to experts, a trained graduate student could probably achieve this with access to adequate equipment. It is also likely that the range of applications of different nanoparticles will broaden in the coming years, which would make this technology more accessible.

For the foreseeable future, experts felt that this technology is primarily within reach of potential state programs, or possibly rogue scientists working within such programs, also because terrorists are much more likely to employ cruder bioweapons than to embark on this complicated technology path.

While the various technology scenarios discussed in the risk part of this report would currently be very difficult, but not entirely unattainable, for non-state actors, most issues – if the path is chosen and the necessary research undertaken – are well within the capabilities of states and large organizations with the necessary resources. However, there are connections between the two types of actors, and military research and development efforts could likely spill over to other actors and sectors of society, as suggested by the historic record of other technology developments.

Nature and Dimension of Risks

In the short term, experts felt, it is highly unlikely that non-state actors would choose the nanotechnology path over easier means of acquiring and employing bioweapons, but that it is possible in specific cases in the medium term, as the underlying technologies will mature. There could be a significant risk of nefarious applications in the longer term. While the tools and techniques are currently not within reach of small groups, some of them are certainly within the capabilities of states in the short to medium term, should the path be chosen.

Nanobiotechnology offers a multitude of potential risk scenarios of varying likelihood and potential consequence. Like synthetic biology, nanobiotechnology currently does not constitute an entirely new dimension to the bioterrorism threat; instead, it was largely viewed as a means to create more potent, nano-enabled bioweapons. Participants agreed that nanobiotechnology might afford methodologies, from the simple to the highly complex, that would make it possible to use agents previously not considered as bioweapons by attaching them to nanoparticles.

Nanotechnology was also recognized as a potential means of facilitating weaponization – for example, by enhancing the environmental stability of biological agents in such a way that the reliability or environmental robustness is increased, potentially making such agents more attractive in the medium to long term.

The possibilities offered by nanotechnology to circumvent certain defense and detection measures were noted as well. The risk posed by nanotechnology is probably greater than that of synthetic biology with respect to spoofing detectors for a variety of reasons: synthetic biology uses biological material, whereas nanotechnology may use inorganic materials to mask biological ones in ways that are beyond the detection capabilities of most systems. Secondly, because nanotechnology represents such a vast range of capabilities and materials, it could potentially be used to develop a wider range of materials or methods to circumvent detectors and other defense measures.

Experts felt that because nanobiotechnology is such a diverse field comprising a range of materials and methods, gauging the risk and threat precisely is an extremely complicated undertaking. There is no single entity or technique that can be singled out as the sole or even major area of concern. This makes devising and implementing domestic and international regulations significantly more complicated.

Dual-Use Potential and Implications for Bioweapons Proliferation

Workshop participants concluded that also in the case of nanotechnology the proliferation of general knowledge and equipment can no longer be stopped, as it has already occurred, although specialized weapons-related knowledge has probably not yet spread. Across the globe, there is a huge industrial push for development, and within political circles, it has become a matter of prestige to have a stake in the promising future of nanotechnology, which is reflected in the large public and private investments into the technology.

Undoubtedly, there is also an extensive dual-use problem in nanotechnology, as materials and equipment as well as many beneficial developments could be exploited for nefarious purposes, such as the above-mentioned nanoparticles. Almost every security-risk potentiality discussed during this project can be derived from completely legitimate research projects and developments, and their adaptation for nefarious purposes was said to be quite straightforward in most areas. The differentiation of peaceful from hostile applications in these areas is hard, if not impossible, and future advances in nanotechnology will likely further complicate efforts against proliferation.

Due to the inherent dual-use nature of developments in nanotechnology, the risk of applying good practices to bad ends will also rise. As the discipline matures and becomes more reliable, pathogens could possibly be nano-engineered, which leads to novel possibilities in designing bioweapons. Nanobiotechnology might be misused to remove the current technical and operational difficulties of a bioweapons attack, such as detection modalities, controlled release problems, or environmental factors that diminish the effectiveness of an attack.

This could have the negative impact of making bioweapons more desirable and could thus make their proliferation and eventual deployment more likely. Potential problems were seen as most likely arising from state weapons programs or maybe smaller actors as the technology becomes more widespread and accessible.

E. Potential Perpetrators: Motivations to Use Synthetic Biology and Nanobiotechnology

Experts also considered some possible motivations for non-state and state actors to use synthetic biology or nanobiotechnology to acquire or modify biological agents that could be used as weapons. The nature of a particular scenario affects the types of actor that are capable of, or interested in, pursuing them. Intent, expected outcome, the ability to overcome obstacles, and the level of technical sophistication might attract or exclude certain kinds of actors.

As regards the required and available capabilities of non-state actors, it was argued that weaponizing synthetic or nanobiotechnology would currently be very difficult, but not entirely unattainable for them. While they currently would likely resort to easier and cruder means of developing and employing a biological weapon with possibly similar effects, technical progress in the coming decades might actually reverse this situation, with synthetic biology lowering the barriers and opening the vast field of biology to "non-experts".

The emphasis on the importance of understanding the motivation aspect of the terrorism problem highlights the need for greater interdisciplinary interactions. Biologists, chemists, and engineers need to interact to a greater extent with political scientists, anthropologists, and cultural experts. It is ultimately the intelligence community's task to assess the aims and interests as well as the capabilities of those who might want to use biology to cause harm.

Non-State Actors

Terrorist Groups

Terrorist groups may find the fear induced by the use (or threat of use) of a biological weapon a useful tool in pursuing their strategic objectives. The use of these weapons might also undermine a population's faith in the ability of its government to protect and govern the country. The resources and technology available to the group will likely define the approach they would need to take to acquire these weapons. Advances in modern technology might provide them with additional avenues to obtain these weapons and increase the potential impact of an attack, thereby enhancing their desirability.

Experts were able to identify a certain number of desirable characteristics that advanced biological weapons might confer as compared to both traditional agents and more conventional weapons, but were not convinced that the advantages were so great as to overcome challenges in the resources, knowledge, time, and complexity that would likely be required over the short to medium term. Experts noted, however, that in the long term, synthetic biology and nanobiotechnology might well lower the barriers to the acquisition and use of biological weapons.

It was recognized that there are probably other options currently available at the lower end of the technological scale, and the historic record of bioterrorism is clearly affected by failures of terrorist groups to successfully weaponize even much simpler agents. As the discussed advances are certainly in the domain of cutting-edge high technology, it is unlikely that terrorist groups will be capable anytime soon of resorting to these kinds of technologies, certainly not without some kind of state support.

Religious Sects

For militant religious sects, especially those with apocalyptical visions, instigating a catastrophic biological attack might be consistent with, and indeed help to further, their religious ideology and could be deemed to be the will of God.

Notions of “constructing life” or “playing God” that are inherent in synthetic and nanobiotechnology, and the potential desire of religious cults to act in the name of God, may impact the likelihood of such a group choosing to use an advanced biological weapon.

However, such actors are no more likely to be able to overcome the technical challenges in the short to medium term than terrorist groups, and the above assessment of capabilities also applies to them.

Rogue Scientists and Individuals

In addition to those with political or religious motivations, individuals with sociopathic tendencies may be prompted to seek biological weapons to harm society or individuals. This becomes a particular concern when the individual has access to many of the necessary resources, e.g., a highly trained biologist who works in a modern biological laboratory with access to pathogens (i.e., a laboratory insider). By increasing the number of individuals who will be able to make use of biology, the likelihood of such events may grow in line with advances in synthetic and nanobiotechnology.

A similar scenario of concern is that of a biologist offering his skills to malevolent ends. As a report compiled by the WMD Commission of the US Congress noted, we “should be less concerned that terrorists will become biologists and far more concerned that biologists will become terrorists”.[49] In this context, the issue was briefly raised during the workshop that there had been some statements from terrorist “leaders” in the past, calling for scientists to use their skills in the pursuit of such groups’ aims, thereby explicitly referring to biological and other unconventional weapons.

Another concern is that of an individual who creates a bioengineered organism out of curiosity or to demonstrate the technical skills, without necessarily having malicious intentions.[50] In the long term, advances in synthetic biology and nanobiotechnology might empower rogue individuals with a desire to “prove what is possible” – analogous to the field of computer technology – that could increase the risk of ill-considered or dangerous experimentation with potentially hazardous consequences.

Organized Crime

Organized crime might develop strong economic and operational incentives in the future to make use of synthetic biology metabolic pathway engineering approaches to produce narcotic drugs or counterfeit pharmaceuticals more easily, cheaper, and in large quantities. In theory, a black market for synthetic biology products might arise.

The buildup of a synthetic biology expertise and infrastructure in this process, and the inherent criminal characteristics of such illegal networks, might make it possible for acquired capabilities to be used or made available to manufacture bioweapons.

State programs

Finally, there is also the threat of state-run biological weapons programs that exploit advanced synthetic and nanobiotechnology techniques to overcome previous technical and operational obstacles. Such programs could use synthetic and nanobiotechnology in pursuit of international or regional power, as a deterrent, or as a force multiplier. States could also apply synthetic and nanobiotechnology to create special operations or assassination weapons. All of these considerations could spur a biological arms race.

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[49] Commission on the Prevention of WMD Proliferation and Terrorism. 2008. World at Risk. Vintage Books: New York, p. 11.

[50] See also J.B. Tucker and R.A. Zilinskas. 2006. The Promise and Perils of Synthetic Biology. In: The New Atlantis, Spring 2006, pp. 25-45.

Although the project focused on non-state actors, experts felt that the role of states cannot be ruled out. While realization of the various technology scenarios discussed in the risk part of this report would currently be very difficult, but not entirely unattainable for non-state actors, most issues are – if the path is chosen and the necessary research undertaken – well within the capabilities of states and large organizations with the necessary resources.

As noted by experts, there is a well-documented history of states diverting every major advance in biology from its original intended purpose to be misused for the development of biological weapons. In addition, there are connections between the two types of actors, and military research and development efforts could likely spill over to other actors and sectors of society, as suggested by the historic record of other technological developments.

Experts argued that some states have motives to look into such issues, and the incentives might even increase over time as bioweapons may become more desirable due to the possibilities offered by the ability to engineer biological systems. Most notable among them are the possibilities that bioweapons could be made more selective and controllable, which would increase their tactical value, and that some of the current operational difficulties of their employment, such as environmental degradation, could be removed.

In addition, the universal dual-use problem in bio- and nanotechnology as well as the vast grey area between defense- and offense-related bioweapons research make it hard to pinpoint actors’ motives and the nature of respective research activities – a well-known problem that is certainly not alleviated by advances in bio- and nanotechnology. The suspicion that potential adversaries could go down such a path provides strong motives for other countries to consider such options as well.

Experts noted that the nature of advances in bio- and nanotechnology as well as the consequences of the ability to engineer bioweapons as desired could challenge current arms control norms and instruments, in particular the Biological Weapons Convention (BWC).

Part 3

Response Options: Towards a Culture of Awareness in Responsible Biotechnology

The threat of malevolent applications of synthetic biology and nanobiotechnology is not immediate. The security implications seem to be marginal in the short term, while a certain level of risk is possible in specific cases in the medium term. In the longer term, however, there could be a significant risk of nefarious applications, which clearly requires a policy response that goes beyond current efforts. It became apparent in our deliberations that the fields of bio- and nanotechnology are still poorly addressed by systematic, nationally and internationally harmonized mitigation activities, rules, and oversight mechanisms.

The following sections provide an overview and assessment of potential governance options and response measures to address some of the challenges that were identified in the first part of this report. The selection of topics is not comprehensive and does not offer a complete picture of available options; instead, it reflects core areas that were emphasized by our expert panel during the second project meeting.

One of the main outcomes shared by the majority of participating experts as well as other observers is that “traditional” arms control measures such as treaty regimes and export control efforts are not best suited and able on their own to cope with the challenges stemming from these technologies. While international arms control agreements and norms will continue to play an important role, the increasing penetration of society by biotechnology, including the emergence of a subculture outside traditional confines, clearly warrants a broader policy response to tackle the wider societal aspects and impacts. Instead of only trying to control and deny access through international arms control measures, experts emphasized that the focus of securing biology should be shifted towards developing a shared responsibility between policy-makers, scientists, and technologists, as well as society at large.

This requires building a worldwide culture of awareness in responsible biotechnology, which in turn requires trust between the various actors. The community of actors must move away from the idea of being able to fully control the risks towards living with them, managing them, and reinforcing a culture of safety and security to minimize the risks by engaging relevant communities and empowering various actors to detect and report abuses. Experts recognized, however, that community action and engagement is not sufficient in all cases. There must also be a sensible legal and regulatory framework to enable the interdiction of those that intend to acquire and use biological weapons and to punish them appropriately, as well as credible obligations of states to refrain from malevolent use.

What is required is an integral web of bottom-up (community engagement; self-governance) and top-down approaches (arms control; laws and regulations) in a national and international context under the broad involvement of various stakeholder groups. The kind of overarching governance model that could weave together such a web of different approaches on different levels and provide the necessary flexibility, as identified by experts, is a networked approach of various types of measures, activities, initiatives, and checks by diverse actors in different areas of intervention, tailored to the needs of the respective communities.

These remarks apply to the entire field of biological science and technology, and most of the following response issues, while tailored to synthetic biology and nanobiotechnology and apart from a few peculiarities, are applicable to biotechnology in general. In fact, it was felt that many of the initiatives that are being undertaken for and by the synthetic biology community could serve as an example for similar activities in other areas of biology. The field of nanobiotechnology was mainly approached through the lens of biotechnology, although it could also have been addressed in the context of nanotechnology. While we touch on the latter on several occasions, it was not a focus for the project and features some specific aspects that could not be considered.

State bioweapons programs have been previously identified as a major source of concern with regard to the malign application of biotechnological advances and surely require a more top-down approach if they are to be addressed appropriately. The following remarks refer to this problem dimension occasionally, but again, workshop deliberations did not concentrate on this issue. Furthermore, discussions did not go into the details of national regulatory and legislative issues.

The next section outlines the characteristics of a networked approach to address the security implications of progress in biotechnology. This is followed by several more concrete response elements that are, as emphasized by experts, important components of such a web of activities. These include: outreach, education, and awareness-raising; codes of conduct and screening frameworks; international arms control and non-proliferation; and technical response measures enabled by synthetic biology and nanotechnology. The subsequent section characterizes the amateur biologists movement, outlines some of the main concerns commonly associated with it, and discusses options for addressing them.

A. The Networked Approach: Establishing a Web of Prevention

A key theme during the workshop was the concept of a networked approach of various measures and resources on different levels to manage the dual-use potential of biotechnology. A networked approach depends upon the energies of diverse stakeholders operating on multiple levels and across all countries to help ensure that the tools of modern biology are used exclusively for peaceful and productive purposes. Such an approach, it was argued, is vital due to the fact that the knowledge, equipment, and techniques needed to exploit these technologies are already widely distributed. Moreover, rapid advances in synthetic biology promise to lower the barriers to the application of biology as technology and extend the availability of tools to an ever-greater number of individuals.

Therefore, unlike the threat posed by chemical and nuclear weapons, addressing the threat posed by biological weapons depends as much on finding "ethical, moral, and social solutions" as it does on restricting accesses to dangerous knowledge and materials. At its foundation, a networked approach means adopting a "human-centric", "community-based" approach to biological security that flexibly takes into account the full range and scope of potential users and their life science activities.[51] The International Committee of the Red Cross (ICRC) has referred to this approach as the "web of prevention" in the context of its "Biotechnology, Weapons and Humanity" initiative.[52]

Shortcomings of Traditional Arms Control Approaches

From the outset of the workshop, experts emphasized that conventional arms control regimes are not sufficient for addressing the full scope of the threat posed by biological weapons. Such regimes, for example those that prohibit the use of chemical and nuclear weapons, are traditionally linear and hierarchical in nature and depend primarily on technical solutions for monitoring installations and arsenals and mitigating proliferation. They aim to determine, through various verification strategies, the relevant technological capacity of states, where it is located, and how it is being used. Although this approach is practical in the nuclear context, for instance, which is highly dependent upon scarce infrastructure, materials, and expertise, it is impractical in the biological context

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[51] Piers Millett. 2010. The Biological Weapons Convention: Securing Biology in the Twenty-first Century. In: Journal of Conflict & Security Law, Vol. 15, No. 1, pp. 25-43.

[52] Cf. www.icrc.org/Web/eng/siteeng0.nsf/html/5VDJ7S.

because the knowledge, technologies, and tools are so widespread. No government or international organization could effectively monitor the tens or hundreds of thousands of small biotechnology facilities worldwide. Experts agreed that this is a problem that needs a “collective, multifaceted, and multidimensional approach”.[53]

On several occasions throughout the workshop, experts expressed that, in many ways, containing the biological weapons threat has more in common with cyber security than with measures in place to address the risks posed by other unconventional weapons. Like cyber threats, the threat of bioweapons is diffuse and far-reaching, largely falling outside the remit of states’ capabilities to monitor, detect, and deter. Some experts also noted that the field of nanotechnology features very similar characteristics and that it might be useful to consider the feasibility and implications of adopting a networked approach to address the security and dual-use challenges in this technological field, as well.

Towards a Human-Centric Network Approach

Recognizing the peculiarities of the biological weapons threat, the Biological Weapons Convention (BWC) has adopted an “evolved network approach” to biosecurity.[54] This approach, although it has a good deal in common with traditional arms control strategies, emphasizes the importance of reaching out to diverse stakeholders, including other international organizations, the private sector, professional and scientific bodies, academic institutions, and others, in an effort to influence the culture of the life sciences and the behavior of life science practitioners.

In recent years, the BWC’s Implementation Support Unit (ISU) has endeavored to fulfill this objective in a number of ways, including participating in a broad range of international workshops and conferences, in an effort to spread the dual-use message and discuss ways in which professional and amateur biologists can help to ensure biological research is done safely, securely, and solely for beneficial purposes. The ISU has also repeatedly invited individuals with a broad range of expertise to the biannual, intersessional meetings of the BWC to discuss the societal implications of modern biology, including synthetic biology. Although “far from perfect”, the BWC’s current strategy is “tailored to the specific nature of biology, is all-inclusive, open, flexible, resilient and robust,

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[53] Cf. Statement to the Conference on Disarmament by Ambassador Masood Khan of Pakistan, President of the Sixth Review Conference of the BWC and Chairman of the 2007 BWC meetings. 7 August 2007. www.unog.ch/80256EDD006B8954/(httpAssets)/1AB706B8AE4A1906C1257330003720F3/$file/Pakistan_1077.pdf.

[54] Cf. Piers Millett. 2010. The Biological Weapons Convention: Securing Biology in the Twenty-first Century. In: Journal of Conflict & Security Law, Vol. 15, No. 1, pp. 25–43.

as well as increasingly human-centric and community-based."[55]

Although the BWC is an important node in the networked approach envisioned by experts to defend against the hostile use of biotechnology, addressing the full scope of this threat cannot entirely (or even mostly) be addressed within the framework of the BWC itself. A truly human-centric, community-based approach to biosecurity, experts emphasized, depends upon empowering those individuals who "do biology" on a daily basis, including, most significantly, life scientists, but also science regulatory bodies, oversight committees, review boards, and similar bodies, to set the standards of good practice and govern the limits of what is and what is not acceptable life science activity.

Thus, the networked approach envisioned by experts is one that harnesses the capabilities of existing international institutions, like the BWC, but draws on, and indeed depends on, the scientific community to take a leading role in securing biology. "Securing biology is not a simple task. It is not something those outside biology could, or should, do alone. Equally, this is not something that biologists can do by themselves […]. This is a truly interdisciplinary problem – one that means we will need to work together, in new ways, with new partners, to find an approach that provides benefits for all."[56]

Although this may, at first glance, seem to be a fuzzy prescription for defending against the nefarious use of modern biology, it is, in fact, a pragmatic approach to biosecurity that draws on and channels the existing motivation and expertise of those who are most intimately involved with the sustainable use of science. Indeed, as recent experience with synthetic biology demonstrates, many of the incentives for the scientific community to contribute actively to such a network are already in place, which has encouraged individuals and groups engaging with these issues of their own accord, as the following sections in this report show.

DNA synthesis companies, for example, have voluntarily taken up the task of screening for genelength sequences of agents of concern. The do-it-yourself biology community has also openly stated its commitment to "openness and safety" and its interest in developing a "code of ethics" and "responsible oversight". These are just a few of the initiatives that are currently coalescing into a foundation for the type of biosecurity network envisioned by experts.

To facilitate the development of a networked governance-model, a "5P-strategy" was proposed and presented during the workshop that would focus on five

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[55] Ibid., p. 42.

[56] http://2010.igem.org/Security/.

points for policy intervention, mainly but not exclusively with regard to DNA synthesis: the principal investigator, the project, the premises, the provider/purchaser (of genetic material), and the public.[57] At each intervention point, several biosecurity measures are conceivable, such as awareness-raising, education and training, codes of conduct, regulation, national laws, and international treaties.

Need for a Common Vision and Common Strategy to Secure Biology

Challenges to establishing and maintaining an inclusive, cohesive, and productive biosecurity network certainly remain. As experts emphasized, it is necessary to establish “ownership” and “buy-in” at all levels of the network. Researchers, government authorities, biotechnology companies, and others need to accept that they have an integral role to play in securing biology. Although partly promoted by the scientific community itself, broad participation will require greater education and awareness-raising that informs individuals of the dual-use threat and challenges them to seek creative “solutions” to the biological weapons “problem”.

At the same time, balancing top-down and bottom-up interventions is a delicate task: On the one hand, the members of the scientific community must be trusted to take on the responsibilities of governing their science, which requires their active involvement in establishing norms, developing codes of conduct, and remaining vigilant in the face of potential abuses in their field. On the other hand, international organizations, governments, public health bodies, law enforcement communities, and others need to monitor, prepare for, and prevent potential breaches in the network. Moreover, these diverse stakeholder groups must adopt, to the extent possible, a clear and consistent dual-use message that reinforces the beneficial aspects of modern biology while condemning the misuse of the science.

There are many challenges to establishing and maintaining a robust biosecurity network that respects the science and its practitioners while also acknowledging the critical role of various authorities operating on the international, national, and regional levels. The fact that efforts to develop such a network are undertaken, however, is reassuring.

What the international community is missing for such an approach to be fully effective, according to experts, is a common vision to enable concerted action and a common strategy to leverage all resources better. The issue here is not so much a lack of resources or international harmonization, but rather a

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[57] Cf. A. Kelle. 2009. Synthetic biology and biosecurity. From low levels of awareness to a comprehensive strategy. In: EMBO Reports, 2009, 10.

question of pooling and coordinating the various efforts under a common header and towards a common goal. Further discussion, and, ultimately, broad agreement on how best to move forward, were highlighted by experts as important challenges that must be addressed.

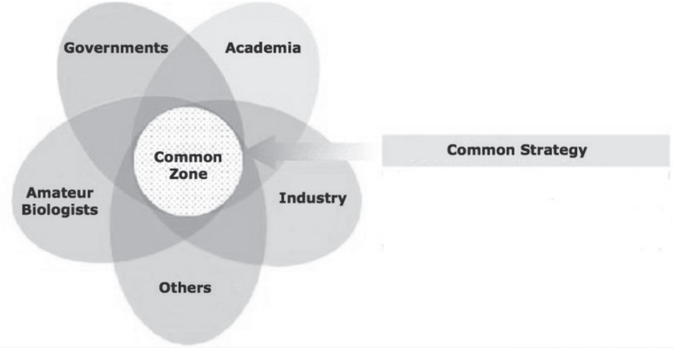

Figure 4. Need for a Common Vision and Common Strategy to Secure Biology

Recommendations

- Elaborate a concept and work towards the coherent establishment of a human-centric, community-based networked approach of existing and new measures and resources on different levels to manage the dual-use potential of biotechnology.
- Reinforce and recognize the value of existing efforts by the relevant communities to consider the implications of their work, thereby taking advantage of existing infrastructure and avoiding duplication.
- To this end, empower individuals engaged in the field; coordinate and integrate existing and new initiatives from various stakeholders; strengthen the science-security link; seek international dialogue on ways to attain a common vision and strategy.
- Support the BWC ISU's adoption of the evolved network approach to biosecurity.

B. Elements of the Networked Approach

1. Outreach, Education, and Awareness-Raising

Throughout the workshop, experts emphasized the importance of enhancing awareness among life scientists as to the dual-use potential of their research, as well as drawing their attention to existing international prohibitions against the deliberate misuse of biology.[58] Such an endeavor, it was argued, depends on strengthening the science-security link and empowering life scientists to take responsibility for their research, as they are best placed to identify how their research might be misused and to assist in taking the necessary precautions to mitigate the potential for such misuse. As the US National Science Advisory Board for Biosecurity (NSABB) has highlighted, “researchers bear the primary responsibility for the integrity of their work,” and thus, “awareness of dual-use research issues by the scientific community [is] fundamental to any successful system of oversight.”[59]

1.1. Low Level of Dual-Use Awareness

The challenge, however, is that life scientists often lack awareness of the biosecurity concerns voiced by security experts, and, where awareness does exist, its importance is often underappreciated. As experts noted, the level of awareness of dual-use issues amongst synthetic biology practitioners, while higher than in other comparable disciplines, remains far from universal, but continues to grow. There is no data available on the dual-use awareness of scientists in nano(bio) technology, but it is presumably much lower, as the field is very diverse and consists of an array of enabling technologies, which hinders community-building and the establishment of communication channels, and has not yet received as much attention from the security community as synthetic biology.

Consequently, experts identified the growing importance of improving the science-security dialogue through targeted outreach activities. Although outreach can take many forms, the general aim is to educate and train researchers,

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[58] Cf. also European Commission. 2007. Green Paper on Bio-Preparedness. Brussels, 11.7.2007, COM(2007) 399 final. And, European Commission. 2008. Synthesis of the Replies to the Green Paper on Bio-Preparedness. Brussels, 04.08.2008, SEC(2008) 2374.

[59] NSABB. 2008. Strategic Plan for Outreach and Education On Dual Use Research Issues: Report of the National Science Advisory Board for Biosecurity; p.1.

research personnel, and research administrators to help them assess and recognize the dual-use potential of their work and to consider options to minimize the risk of their findings being misused or misapplied.

The message can be communicated in a variety of ways, including through print and electronic media, presentations, focus groups, and role-playing exercises. Above all, experts emphasized that outreach activities must be systematic and sustained, ensuring regular communication between the science and security communities, and stressed the lack of systematic education efforts and coordination on the international level.

1.2. Broad Stakeholder Involvement and Tailored Education

A comprehensive outreach strategy requires the involvement of multiple stakeholders educating broadly on dual-use issues at the institutional, regional, national, and international levels. Governments, scientific societies, professional associations, and the private sector all have important roles to play in promoting a culture of awareness and responsibility. Such a strategy, experts argued, requires a mixture of top-down and bottom-up interventions that share a common vision, yet speak to the individual needs of different countries and research communities. In particular, there is a need to acknowledge the social and cultural contexts of individual communities and to tailor the dual-use message accordingly.

In a recent publication entitled "Education and Ethics in the Life Sciences",[60] the authors pointed to the importance of on-going and workplace-relevant instruction on dual-use issues, including responsible conduct of research and laboratory safety training, and also suggested the use of electronic support material that can be fitted into existing education programs such as university curricula and used to raise awareness. In this context, the online portal "Dual-Use Bioethics"[61] of the University of Bradford and other partners was presented during the workshop. Such websites provide relevant resources on dual-use issues, including comprehensive educational modules[62] that are designed to support life scientists and educators in learning about biosecurity and dual-use issues as well as in compiling educational material for students. Experts noted that such initiatives are an important step in reaching out to relevant communities and should be internationally promoted and expanded.

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[60] Brian Rappert (ed.). 2010. Education and Ethics in the Life Sciences: Strengthening the Prohibition of Biological Weapons. Canberra: ANU E Press.

[61] www.dual-usebioethics.net/.

[62] Cf. www.brad.ac.uk/bioethics/EducationalModuleResource/EnglishLanguageVersionofEMR/.

In addition, experts stressed the importance of knowledge management within social networks. Specifically, experts highlighted the importance of bridge-builders, i.e., persons with connections to, and credibility in, two different peer groups – in our case, the biotechnology and security communities. Bridge-builders facilitate effective transfer and absorption of information between groups and provide opportunities to address issues of concern in a forthright manner. In this sense, networks and personal ties should be viewed as strategic resources.

Although much of the emphasis on outreach and awareness-raising focuses on the life science community, experts emphasized that there is a need for broader engagement with other stakeholders, including academia and the public. With regard to synthetic biology, this is deemed to be par-ticularly important not only because of rapid advances in this field, but also because synthetic bi-ology blurs the lines between research disciplines (notably between biology, chemistry, engineering, and computer science) and challenges the notion that practicing science is exclusive to formal research settings with the emergence of a subculture of amateur biologists. Thus, awareness-raising activities in the area of synthetic biology need to address diverse practitioners from different backgrounds who may lack formal institutional affiliations.

Specifically, as the NSABB suggests, education efforts should also engage with: (1) those who are not ordinarily subject to (or the subject of) biosafety and biosecurity requirements; (2) those who are not affiliated with a university or research institution; and (3) students at all levels.[63] Furthermore, as the synthetic biology policy debate proceeds, the NSABB proposes to organize "town-hall style" regional meetings followed by an "intensive educational package", including workshops, presentations, print and electronic materials, exhibits, and other activities that further raise awareness and promote compliance.[64]

The situation in the area of nanotechnology seems to be similar or even worse in that the field is very diverse and comprises a range of materials, methods, and techniques as well as practitioners from different backgrounds.[65] There is no field of study labeled "nanosciences" and few scholars of the biological, chemical, or material sciences, etc. engaged in "nanotechnology" would call themselves "nanoscientists". This fragmentation complicates the identification and junction of a target audience and impedes the development of a tailored

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[63] NSABB. 2010. Addressing Biosecurity Concerns Related to Synthetic Biology: Report of the National Science Advisory Board for Biosecurity.

[64] Cf. NSABB. 2008. Strategic Plan for Outreach and Education On Dual Use Research Issues: Report of the National Science Advisory Board for Biosecurity; p.4.

[65] Cf. M.E. Kosal. 2009. Nanotechnology for Chemical and Biological Defense. Springer Academic: New York.

message. Experts felt that there remains a clear need for significant efforts to raise the awareness of, and develop a sense of responsibility for, dual-use issues within the nanotechnology communities.

1.3. ‘Going Out’ with Key Messages

The US Federal Bureau of Investigation’s (FBI) Bioterrorism Prevention Program that was presented and discussed at our workshops provides a good example of how dual-use outreach activities can be tailored to incorporate broad collaboration while bringing dual-use issues to the attention of diverse research communities, from professional life scientists to amateur do-it-yourself biologists.

Drawing on the outreach and education recommendations put forward by the NSABB, the FBI’s Bioterrorism Prevention Program engages in scientific, industry, and academic outreach on dual-use issues in the life sciences. Notably, the FBI has collaborated with private industry,[66] international organizations,[67] academic institutions and the amateur biology community,[68] institutional animal care and use committees, and institutional review boards and biosafety committees[69] to shed-light on dual-use research issues.

The FBI’s recent work at the 2009 International Genetically Engineered Machines (iGEM) competition, which brings together student synthetic biology research teams from around the world, is indicative of their efforts to engage with young researchers working at the forefront of the life sciences. At the 2009 competition, the FBI, together with the BWC Implementation Support Unit (ISU), prepared a poster exhibit and made a dual-use research presentation that informed teams of the biosecurity issues associated with their research. The FBI also used this occasion to establish an ongoing dialogue between law enforcement and life science research communities, highlighting the importance of communicating research concerns with local field agents.

At the same time, the iGEM competition offered an opportunity for the BWC ISU to introduce the subject of international prohibitions against the deliber-

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[66] The FBI, together with the US Department of State and the United Nations (UN) Biological Weapons Convention’s (BWC) Implementation Support Unit (ISU), hosted an “International Industry Workshop on Synthetic Biology” on 3 November 2009 that addressed ways of improving the biosecurity of DNA synthesis services.

[67] The FBI participated in this “Synthetic Biology and Nanobiotechnology Risk and Response Assessment” project hosted by the United Nations Interregional Crime and Justice Research Institute (UNICRI) in 2010.

[68] The FBI discussed outreach and promoted responsible research and career opportunities at the “Outlaw Biology?” symposium hosted by the University of California, Los Angeles on 29-30 January 2010.

[69] The FBI, together with the Massachusetts Society for Medical Research (MSMR), co-sponsored a “Biosecurity Conference” on 3-4 May 2010 that focused on how research and security communities can work together to address biosafety and biosecurity threats.

ate misuse of biology, reminding students that there has been a long history of biological weapons development and disarmament, as well as helping to place the biosecurity debate in the international context. In addition, teams now have access to a number of online resources that provide valuable information on biosecurity, which can be incorporated into their research projects through the newly established security section on the iGEM website.[70]

The importance of reaching out to life scientists early in their careers, establishing the foundations for a “culture of responsibility”, was deemed to be particularly important by experts participating in the workshop, as was the need to engage broadly with international life science communities. With regard to the former, it has been repeatedly suggested that such efforts should be systematically introduced into the university curricula by developing compulsory courses and learning materials on biosecurity and dual-use issues in order to educate young students alongside their early encounters with biology. Such engagement, it was argued, is critical in light of the growing demand for training in the life sciences and open access to information and equipment that can be used for both productive and destructive purposes.

Thus, the FBI’s outreach and awareness-raising efforts are timely, and the message that is being delivered is in accord with the prevailing opinions of experts. That is, it is critical to nurture robust and productive life science research while minimizing the risks of misuse. Experts agreed that these messages now need to be systematically taken to the international level.

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70 Cf. http://2010.igem.org/Security.

Key dual-use message points

The US National Science Advisory Board for Biosecurity (NSABB) has developed a set of key message points that should be conveyed in outreach briefings and presentations about the dual-use research issue.

1. Research in the life sciences is a critically important national endeavor that yields tremendous benefits to agriculture, medicine, public health, the environment, the economy, and national security.
2. The value of life sciences research notwithstanding, knowledge and technologies in the life sciences have evolved to a point where individuals who intend to apply them maliciously could inflict extraordinary harm to public health, agriculture, the environment, the economy, and national security.
3. Life scientists and others in the research community have an exceedingly important responsibility to minimize the potential for this misuse of the information and technology associated with their research when such potential exists.
4. The dual-use potential of life sciences research is not always immediately evident, and scientists have a responsibility to be mindful of this potential, and handle dual-use information and technologies responsibly. In particular, scientists need to consider the dual-use potential of emerging technologies, such as synthetic genomics and synthetic biology.
5. Scientists should engage – and, where appropriate, educate – others about dual-use research issues. Audiences should include not only their own laboratory staff, but also colleagues, the public, federal officials, and members of Congress.
6. If even only a few scientists fail to attend to their responsibilities to handle dual-use research appropriately, the results could be extremely damaging to public and agricultural health, the economy, national security, and public confidence in science. Therefore, it is incumbent upon life scientists and their professional organizations to initiate and continue dialogue on this matter to maximize awareness and appreciation for the significance of concerns related to dual-use research.
7. The future of research depends heavily on public trust, and even one incident involving the misapplication of dual-use information or technologies could threaten that support and the future vitality of the life sciences enterprise.
8. Perpetrators intent on doing harm will most likely be able to do so; thus, the intent of an oversight system is to assist those who behave responsibly and to avoid inadvertently aiding those who seek to do harm.

Source: NSABB. 2008. Strategic Plan for Outreach and Education On Dual Use Research Issues: Report of the National Science Advisory Board for Biosecurity, pp. 8f.

As the NSABB has highlighted, “[by] definition, ‘outreach’ means going out into the community”[71] , and thus there is a need for education and awareness-raising activities to engage with communities “on the ground” in ways that are context-specific and tailored to the needs of individuals. As discussed in this section, such engagement requires the participation of multiple stakeholders working in diverse areas and across national borders.

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[71] NSABB. 2007. Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information. Report of the National Science Advisory Board for Biosecurity; p. 30.

The resources and expert views shared in this section provide a snapshot of how effective out-reach strategies can be developed, but it is ultimately for policy-makers, security experts, civil society, and others to deliver information on dual-use research issues that is appropriate to the community in question. Although professional life scientists are perhaps most immediately in need of education and training in biosecurity and biosafety, the scope of dual-use awareness-raising should include ever broader communities, including academia, industry, governments, amateur biologists, and the general public, fostering an open forum for discussion and debate.

In this regard, experts repeatedly emphasized the importance of dialogue with the general public and public outreach and education activities in order to inform people about progress in biotechnology and its potential benefits and risks as well as to stimulate a debate on what society wants, what level of risk it is willing to accept, what kind of rules and (ethical) constraints should be set (by whom), etc. There has been almost no such systematic public debate at all so far with regard to synthetic biology (and nanotechnology), even though public awareness is crucial for bridging the apparent disconnect between public and community expectations and gaining public trust as well as for avoiding misinformed political backlash in case of a detrimental incident.

Recommendations

- Develop a comprehensive outreach strategy for systematic outreach to life science communities and work with them to address dual-use issues of concern.
- Reach out to international partners and foster systematic education efforts and coordination on the international level.
- Also target non-biologists, such as engineers, computational modelers, mathematicians, etc. specifically.
- To this end, seek the support of community peers; foster dialogue between stakeholders; carry the dual-use message to various community events; support or organize events and educational programs specifically pertaining to biosecurity; systematically enter university and other curricula and reach out to life scientists and lab staff early in their careers; ensure the existence of, and promote, web portals with e-learning modules and information on dual-use and biosecurity issues tailored to the needs of various stakeholder communities.
- Foster broader engagement with the general public on the benefits and risks of advances in bio- and nanotechnology, including synthetic biology, and enable a public debate on what society wants, what level of risk it is willing to accept, what kind of rules and (ethical) constraints should be set (by whom), etc.

2. Codes of Conduct

One approach towards educating and raising the general awareness of scientists repeatedly discussed in the framework of this project is to develop codes of conduct that address biosecurity or dual-use concerns. While the life sciences have an array of different codes with diverse objectives and target audiences, such codes generally attempt to influence the thinking and behavior of pro-fessionals involved in a given field.

Codes of conduct are located at the intersection of science, society, and government with the underlying objective and assumption that scientists have a special responsibility with regard to the dual-use potential of their work and the misuse of science and technology. A code of conduct constitutes a non-legislative form of control that is, apart from social in-group pressure, voluntary by definition and ideally community-derived.

The bottom-up approach is important because, on the one hand, the involvement of practitioners ensures the actual relevance of the elaborated norms in day-to-day activities; and on the other, autonomous self-regulation fosters a sense of ownership, responsibility, and credibility, which may make adherence more likely. As an additional incentive for affected communities, it may, if successful, forestall the top-down imposition of legal research restrictions. While governments have some role in fostering and facilitating the elaboration and adoption of codes of conduct by scientific peer groups, the primary actors are the scientific communities.

The worldwide network of science academies, the InterAcademy Panel (IAP), published a set of principles intended to guide the development of scientific codes of conduct in the field of biotechnology. The statement on biosecurity, endorsed by 68 national science academies, contains five principles that call on scientists to do no harm and foresee and prevent potential harmful con-sequences of their research; to follow laboratory biosafety and biosecurity procedures; to educate themselves and teach relevant national and international laws, regulations, and policies aimed at preventing the misuse of biological research; and to raise their concerns with authorities in case harmful activities are suspected.[72]

In a similar, though more comprehensive manner, the US government's National Science Advisory Board for Biosecurity (NSABB) published a set of considerations for the development of a code of conduct for dual-use research in the life sciences. These considerations do not provide concrete rules to be followed,

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[72] InterAcademy Panel (IAP). 2005. IAP Statement on Biosecurity.

but include various provisions with the overarching imperative of considering dual-use issues at various stages of the research process.

The fundamental principle states that "individuals involved in any stage of life sciences research have an ethical obligation to avoid or minimize the risks and harm that could result from malevolent use of research outcomes."[73] Towards that end, scientists are encouraged to assess their own research for dual-use potential; to stay informed about relevant issues; to train others to identify and deal with dual-use research; to serve as role models of responsible behavior; and to be alert to potential misuse of research.[74] These fundamental principles are further elaborated for various research stages, settings, and actors. Although no direct reference is made to any specific research field, it is obvious from our discussion of the security risks and implications associated with synthetic biology and nanobiotechnology in the previous section that the NSABB's considerations are of direct relevance for the two emerging technology fields.

Numerous attempts to draft codes of conduct for the biosciences and related subfields have yielded mixed results, with many observers questioning their practical utility and adequacy as policy options. Codes of conduct have been criticized for "being vague, open to multiple interpretations, ineffective to stop those with ill intent, of uncertain or questionable practical worth, and often poorly known within professional communities".[75] On the positive side, codes of conduct help to raise awareness about sensitive issues, foster the creation of standards, clarify responsibilities, and increase public confidence. In addition, estimating the effectiveness of codes of conduct by assessing only their content and implementation underestimates the importance of the evolving process of devising and making codes of conduct meaningful, which is probably just as important.[76]

Workshop participants felt that even though codes of conduct are limited in scope and effect, they are relevant and have a legitimate role to play. In light of the majority opinion that controlling access to knowledge and equipment in bio- and nanotechnology is probably not feasible anymore because it is so widespread already and that a top-down approach does generally not seem to be an effective way of tackling many of the challenges posed by modern biotechnology, it is becoming increasingly important to concentrate on people and

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[73] NSABB. 2007. Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information. June 2007, p. 47.

[74] Ibid.

[75] Brian Rappert. 2007. Codes of Conduct and Biological Weapons: An In-Process Assessment. In: Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science Volume 5, Number 2, p. 2.

[76] Ibid.

the way they think about issues of societal concern, and to find better ways for stakeholders to work together.

In this respect, codes of conduct – as a part of a web of activities – can serve important functions in transparency, dialogue, education, and awareness-raising as well as in bridging the disconnect between the science and security communities and society at large. However, codes of conduct need to be well applied and adhered to as broadly as possible, while the actual outcome and eventual success is hardly steerable from the outset. Experts stressed the fact that such softer bottom-up approaches cannot succeed by themselves, but need to be complemented by investments, individual engagement, and community impetus. In order for them to be effective, all available resources must be leveraged and all relevant stakeholders be engaged as broadly as possible.

Going one step further, some experts suggested that the concept of codes of conduct in biotechnology be taken to the next level by establishing an ethical framework analogous to the Hippocratic oath in medicine. In this context, it was proposed that such a framework be institutionalized; for instance, that biology students would need to pass certain courses devoted to security and ethics or go through some basic training as part of the regular university curriculum. These suggestions point to the general and well-known deficiency in the field of biotechnology that there is no established and systematic professional ethics standard that biologists would "routinely" adhere to.

While many code-of-conduct initiatives pertaining to biotechnology or the life sciences in general would implicitly apply to synthetic biology and to a certain degree also to nanobiotechnology, there are some efforts underway – primarily for the former area – to address the peculiarities of these subfields more specifically. Experts agreed that concerted and systematic efforts should be undertaken to address the awareness gaps, whereas codes of conduct are just one of many possibilities to achieve this objective, but surely have their role to play.

In the following, examples of codes of conduct and similar initiatives with relevance for synthetic biology and nanobiotechnology, including screening frameworks in the DNA synthesis industry, are referenced and briefly discussed.

2.1. Code of Conduct Initiatives in Synthetic Biology

In synthetic biology, a number of proposals pertaining to the elaboration of a community code of conduct were put forward in recent years. One of the earliest calls to build a safe and responsible community was raised by one of the leading scientists in the field, George Church at Harvard University. He was one of the first to propose that commercial DNA and oligonucleotides orders be screened for similarity to known pathogenic agents and that synthesis instruments and reagents be licensed, accompanied by the setup of a registry database and a governmental clearinghouse for oversight.[77]

Later, he also called for the elaboration of a community code of ethics and standards for biological engineering that would make certain measures standard practice. These included: adherence to laboratory biosafety standards; biological isolation to reduce the viability of engineered biological systems outside the laboratory; building self-destruction mechanisms into engineered cells; and including watermarks in engineered sequences for easier tracking. In the same article, the importance of public outreach was also underlined.[78]

In 2006, at the second international meeting on synthetic biology, SB2.0, participants considered and subsequently rejected a draft code of conduct declaration that supported the adoption of screening procedures as well as the development and consideration of unspecified governance options, while putting greater emphasis on self-governance.[79] The adoption of the code was blocked, not because there were problems with its aims or objectives, but because certain participants felt further outreach and engagement was needed first.

These and successive deliberations have yet to lead to the adoption of a community code of conduct. However, experts participating in our workshops agreed that compared to other actors in biotechnology and other emerging technology fields including nanotechnology, the synthetic biology community shows a clear willingness to engage in an ethics, safety, and security dialogue and is even proactively initiating important developments and discourses in this regard. Assuming that such engagement continues and leads to sustainable results, many experts felt that the synthetic biology community could serve as a model for other disciplines in the responsible pursuit of science and technology.

A case in point is how safety and security issues are dealt with within the framework of the International Genetically Engineered Machine competition (iGEM), an undergraduate synthetic biology competition intended to draw young academics into the field. In the 2010 competition, completing a short biosafety questionnaire was a condition of participation. Judges assessed the teams' compliance with this requirement during the end of year jamboree and created a special award for excellence in biosafety and biosecurity.

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[77] George Church. 2004. A Synthetic Biohazard Non-proliferation Proposal. http://arep.med.harvard.edu/SBP/Church_Biohazard04c.doc.

[78] George Church. 2005. Let us go forth and safely multiply. In: Nature, Vol. 438, 24 November 2005, p. 423.

[79] Declaration of the Second International Meeting on Synthetic Biology, Berkeley, California, USA, 29 May 2006. http://openwetware.org/wiki/Synthetic_Biology/SB2Declaration.

Not only are participating teams required to think about and document possible biosafety issues associated with their project,[80] but they are also encouraged to look at aspects of “human practice” in synthetic biology as part of their project, such as ethical, economic, environmental, legal, and social issues of concern. In 2009, for instance, the iGEM team from the University of Beijing conducted a field survey with 17 Chinese biotech firms to see whether they would deliver equipment and materials, some of which had a hazardous potential, to a student’s home address. They were surprised to see how easy it was and that only one company rejected their order. This led them to conclude that not enough attention is paid to certain areas and that transactions of certain biological materials must be regulated.[81] Experts were surprised to learn that the orders were so easily accepted with virtually no difficulty. They were impressed by the community’s own initiative to reveal these deficiencies and, at the same time, wondered about the passivity of governments.

In addition to issues of biosafety and human practice, iGEM participants are also increasingly made aware of biosecurity concerns and are encouraged to think about the potential for misuse of their work on a voluntary basis. In 2010, for example, one team from ENSIMAG, a French engineering school, and from Virginia Tech University developed a suite of screening software for use by the synthesis industry. They used the software to screen the iGEM gene sequence database for dangerous entries and demonstrated that only one sequence in the registry was of specific interest, and that it had already been identified and flagged as such.[82]

It is also planned to draft a code of conduct for the iGEM competition “that everyone involved would commit themselves to. Such a code could help ensure that we think about security as something that does directly involve us, is part of our project and can be dealt with in a way that helps us to get on and have some fun engineering biology.”[83] Participating teams are invited to think about what they are prepared to accept and to provide their input on the content of such an iGEM code of conduct.

Representatives of the amateur biologists community are also working towards the elaboration and adoption of a code of conduct for the community; they are currently assessing the situation, gathering input, and exploring neces-

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[80] Cf. http://2010.igem.org/Safety.

[81] http://2009.igem.org/Team:PKU_Beijing/Human/Survey.

[82] http://2010.igem.org/Team:VT-ENSIMAG_Biosecurity; http://2010.igem.org/Team:VT-ENSIMAG/Registry.

[83] http://2010.igem.org/Security.

sities and options regarding such a code (see also the section on amateur biology below).[84]

Recommendations

- Foster and actively support concerted and systematic efforts to develop code of conduct values, principles, and standards for dual-use research in the life sciences by individual communities, including synthetic biology and nanobiotechnology.
- Promote and actively support the broad adoption of codes of conduct through information and outreach activities as well as with financial and political leverage.

2.2. Codes of Conduct in the Gene Synthesis Industry: Screening Frameworks

The efforts of the gene synthesis industry are another strong example of the proactive and responsible engagement of the synthetic biology community on the implications of their work. With the emergence of enhanced technological capacities and increased media coverage of synthetic biology, gene synthesis became increasingly visible as a key technology with an obvious dual-use potential.[85] This resulted in a range of initiatives designed to create a safe and sustainable environment for commercial gene synthesis. These measures include guidelines for the safe and secure processing of orders for synthetic genes with a clear focus on biosecurity.

These so-called screening procedures constitute a technical code of conduct that generally stipulates the screening of gene orders against a pathogenic DNA sequence reference database as well as the screening of customers in order to verify their identity and affiliation. If “red flags” are raised during the two-tiered, partially automated screening process, a human expert should conduct follow-up checks and subsequently notify the authorities in case security concerns persist. There are currently three major sources of guidance – one from the U.S. government,[86] another from the International Association Synthetic Biol-

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[84] Cf. http://diybio.org/safety/; and www.prnewswire.com/news-releases/responsible-science-for-do-it-yourself-biologists-97362669.html.

[85] Cf. “Revealed: the lax laws that could allow assembly of deadly virus DNA – Urgent calls for regulation after Guardian buys part of smallpox genome through mail order”, The Guardian, June 14, 2006. http://www.guardian.co.uk/world/2006/jun/14/terrorism.topstories3.

[86] US Department of Health and Human Services. 2010. Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA. www.phe.gov/Preparedness/legal/guidance/syndna/Documents/syndna-guidance.pdf.

ogy (IASB),[87] and the last from the International Gene Synthesis Consortium (IGSC).[88] The cost burden of these voluntary procedures for individual companies is bearable but increasing, according to industry representatives.

In a 2007 report by the J. Craig Venter Institute (JCVI), the Massachusetts Institute of Technology (MIT), and the Center for Strategic and International Studies (CSIS), a variety of governance options pertaining to DNA synthesis with a main focus on commercial activities were comprehensively discussed and assessed. The authors concluded that the hybrid approach of screening DNA orders in conjunction with verifying the identities of people who place orders is the most effective option for denying a potential bioterrorist access to commercially available DNA and preventing biosecurity incidents.

Other measures identified in the report that focus on the availability of equipment and the activities of users with a lower but moderate effectiveness include the registration and licensing of materials, equipment, and DNA synthesizers, as well as increased education about risks and best practices, broader review and oversight of experiments of concern, and the compilation of a manual on biosafety in synthetic biology laboratories.[89] None of our discussions held at either project meeting suggested that there had been any significant changes that might affect the validity of this analysis.

2.2.1. Private Screening Initiatives

One of the first initiatives to draft a code of conduct for commercial DNA suppliers (and other interested actors) was initiated in 2007 by the International Association Synthetic Biology (IASB) in Germany. The code was drafted in an open process, leading to the formal adoption of the “IASB Code of Conduct for Best Practices in Gene Synthesis”[90] by eight international companies in 2009. The code emphasizes commercial operations, but is not restricted to the corporate sector and can be adopted by other actors, such as research institutes or academic institutions.

In essence, the IASB Code contains commitments to screen all gene synthesis orders that are larger than 200 base pairs (bp); to take reasonable steps to confirm the identity of customers and categorically refuse delivery to private addresses; to keep records of suspicious inquiries and positive screening

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[87] www.ia-sb.eu/tasks/sites/synthetic-biology/assets/File/pdf/iasb_code_of_conduct_final.pdf.

[88] www.genesynthesisconsortium.org/Gene_Synthesis_Consortium/Harmonized_Screening_Protocol.html.

[89] M. Garfinkel et al. 2007. Synthetic Genomics – Options for Governance.

[90] www.ia-sb.eu/tasks/sites/synthetic-biology/assets/File/pdf/iasb_code_of_conduct_final.pdf.

hits for forensic purposes; to cooperate with authorities and provide them with evidence; and to engage with the synthetic biology community for the further development and optimization of the code. The IASB also formed a Technical Expert Group on Biosecurity (TEGB), which regularly reviews the implementation of biosafety and biosecurity measures as well as technical aspects and definitions of the IASB code of conduct. The TEGB has also been tasked with developing an IASB-operated seal of approval program to certify compliance with the code of conduct.

In a very similar manner, the International Gene Synthesis Consortium (IGSC), an association of currently five mainly US-based gene providers, drafted its "Harmonized Screening Protocol" in 2009.[91] The IGSC screening protocol is based on similar principles and procedures as the IASB code of conduct, albeit with an exclusive focus on industry practices. This led some experts to wonder why the two associations or the companies behind them did not join forces and come up with a common framework. Apparently, a dispute over technical aspects of the standards, the institutional eligibility to define and implement them, and the mechanisms involved prompted a public disagreement between the two groups.[92] A main issue was the question of whether or not a human expert should follow up on hits derived from the automated screening process, although both guidelines currently stipulate this practice, as fully automated screenings are not yet technically feasible.

Experts felt that, given the identical nature of the two arrangements, there seems to be little divergence in substance between the two consortia, and that it is better to have two competing codes than none at all. It was also noted, though, that complying with several standards places additional burdens on companies, especially those that operate across diverse geographical and regulatory boundaries. However, this might just be a transitional step, as there is a tendency for the market to streamline competing standards; and given the nascent nature of the industry, further consolidation in the future is likely.

Although over 80% of gene synthesis orders are currently filled by companies participating in one of these screening initiatives, this still only amounts to around half of the approximately 25 commercial gene providers worldwide. The fact that not all companies perform a screening not only constitutes an economic disadvantage for those that do (albeit a bearable one at the moment), it also makes the screenings that some of them do perform "futile" from a security

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[91] www.genesynthesisconsortium.org/Gene_Synthesis_Consortium/Harmonized_Screening_Protocol.html.

[92] Cf. E. Check Hayden. 2009. Keeping genes out of terrorists' hands - Gene-synthesis industry at odds over how to screen DNA orders. In: Nature, 461, p. 22.

point of view, since a potential perpetrator could simply place orders with a company that does not. Further efforts are required to ensure that these standards are adopted more broadly across all commercial gene synthesis providers, regardless of their geographic location.

With access to the right equipment and knowledge, it is also possible to synthesize genes in an academic setting. According to experts, there is less awareness of, and focus on, dual-use issues outside of the commercial realm, and it would be desirable to encourage those in this position to be included in a broader gene synthesis conduct framework as well (either inside or outside of existing bodies).

Given the need for a diverse engagement on this issue, in terms of both geography and sectors, experts debated whether governments should become more involved and if so, in what form. The question was raised, for instance, whether some kind of basic screening practice should be made a mandatory requirement. This, it was felt, would only make sense if it were an internationally agreed obligation, and would require some sort of compliance monitoring. Experts stopped short of recommending the creation of mandatory screening procedures in light of likely future developments in this area. Universalization, however, would certainly be desirable and a greater focus in the future.

2.2.2. Government Involvement

A first step towards government involvement was taken by the US Department of Health and Human Services (HHS) in November 2009. Following the two industry initiatives, the HHS published its “Screening Framework Guidance for Synthetic Double-Stranded DNA Providers” for public consideration.[93] In October 2010, the final version of the Guidance, including public input, was officially released.[94]

The document is intended to provide guidance to synthetic DNA producers on the screening of orders so as to ensure compliance with regulations and provide a set of best practices. Compliance with the procedures outlined in the guidance is voluntary. All the provisions are again completely congruent with the provisions of the IASB Code of Conduct and the IGSC’s Screening Proto-

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[93] US Department of Health and Human Services. 2009. Screening Framework Guidance for Synthetic Double-Stranded DNA Providers. www.gpo.gov/fdsys/pkg/FR-2009-11-27/pdf/E9-28328.pdf.

[94] US Department of Health and Human Services. 2010. Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA. www.phe.gov/Preparedness/legal/guidance/syndna/Documents/syndna-guidance.pdf. See also the “Response to Public Comments on the Draft Screening Framework Guidance for Synthetic Double-Stranded DNA Providers”, HHS 2010. www.phe.gov/Preparedness/legal/guidance/syndna/Documents/syndna-commentsresponse.pdf.

col. “These guidelines were developed to be easily integrated within providers’ existing protocols with minimal cost, and to be globally extensible […] so that fundamental goals, provider responsibilities, and the screening framework could be considered for application by the international community.”[95]

The issuance of the HHS guidance confirms the direction, value, and legitimacy of the industry initiatives, while leaving room for (international) self-governance to unfold further eventually. If that self-governance should fail to materialize, the basis for additional measures and enforcement is set. Experts emphasized that other governments should become more involved, too.

As a potential alternative to increased government pressure, there are signs that social responsibility factors might come into play more prominently. In line with the fact that such factors – in conjunction with public image considerations – were probably one of the main motivations for the gene synthesis industry to proactively engage in screening efforts, the practice is increasingly supported by influential customers, such as the pharmaceutical industry. One such global player has already stated that it only works with DNA providers that embrace screening standards and help reduce the risk of misuse.

In this regard, the aforementioned seal of approval to certify compliance with a screening framework could become an important label and should be fostered, not only in the industrial domain. Ideally, adhering to a screening procedure would become an economic advantage and could attract customers as well as investors. If successful, such a scheme would also allow government intervention to be kept as low as possible, while relying more on verifiable self-regulation. However, experts stressed that in order to establish the credibility of such a “non-governmental” compliance certificate, it would have to go hand-in-hand with an independent auditing scheme to assess and ensure compliance. Experts mentioned the Forest Stewardship Council (FSC)[96] as a possible model for such a certification and compliance framework.

2.2.3. Technical Issues

All three screening frameworks mentioned above stipulate that ordered gene sequences are screened against a subset of the GenBank[97] sequence database. The screen compares the order against the sequence of certain pathogenic or-

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[95] US Department of Health and Human Services. 2009. Screening Framework Guidance for Synthetic Double-Stranded DNA Providers. www.gpo.gov/fdsys/pkg/FR-2009-11-27/pdf/E9-28328.pdf.

[96] www.fsc.org/.

[97] www.ncbi.nlm.nih.gov/genbank/.

ganisms. These are usually selected on the basis of the organisms on the Australia Group List of Biological Agents for Export Control[98] and/or the US Select Agents[99] list, though the chosen reference lists may vary between companies.

The identification of sequences from listed biological agents is commonly accomplished through the use of commercially available software tools, such as BlackWatch.[100] These tools perform a BLAST (Basic Local Alignment Search Tool)[101] search to compare sequences and offer additional functionalities, such as records keeping. Both GenBank and BLAST are operated and maintained by the US National Center for Biotechnology Information (NCBI) in cooperation with international partners.

The screening procedures are impeded by a high number of false positive hits, because many genes are conserved between pathogenic and non-pathogenic organisms. As a result, an order for a sequence from a non-listed organism could cause a hit if the same sequence is present in a listed agent – even if it does not relate to infectivity, pathogenicity, or any other phenotypic characteristics of security interest. The elimination of these hits causes extra burden to DNA suppliers, and constant efforts are undertaken to improve the database system and tools in order to ensure that a hit is only returned for orders that do pose a security concern.

Other problems related to the detection of pathogenic sequences include: false negative hits, such as orders deliberately split among different providers that, if they had been requested from a single source, would have been flagged as “of concern”, or sequences purposely modified to avoid database matches; and the existence of many legitimate uses for pathogenic sequences, such as the development of vaccines.

The screening frameworks currently only apply to double-stranded DNA constructs. Shorter, single-stranded DNA fragments, so-called oligonucleotides, are not currently screened for pathogenicity, because it is difficult to detect true hits or eliminate false ones with a sufficiently high accuracy due to their short length. The technical hurdles for the synthesis of hazardous bioagents from single-stranded oligonucleotides are higher than from double-stranded DNA fragments, i.e., oligonucleotides bear a “lower” biosecurity risk. With a moderate skill-set, however, a trained molecular biologist can assemble oligonucleotides

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[98] www.australiagroup.net/en/biological_agents.html.

[99] www.selectagents.gov/Select%20Agents%20and%20Toxins%20List.html.

[100] https://biotech.craic.com/blackwatch/.

[101] http://blast.ncbi.nlm.nih.gov/Blast.cgi.

into functional genes, and the respective procedures are becoming easier. While companies that synthesize gene- or genome-length pieces of DNA are clearly a priority in the prevention of misuse, oligonucleotides orders should ideally also be screened for pathogenic sequences. There are efforts underway to improve the technical viability of the respective screening procedures and database tools. However, some experts noted that screening orders of oligonucleotides might be technologically infeasible and would add little security, while placing additional burdens on the industry. As an alternative, it has been suggested that oligonucleotide providers could only perform a customer screening.

The sequence database as well as the quality of the data against which orders are matched are crucial criteria when it comes to avoiding false hits and being able to identify DNA sequences accurately. An effective screening procedure would rely on a database that provides the ability to detect the smallest possible sequence fragments that are of interest to the security community without producing too many false positive hits. Proposed solutions to achieve this include identifying sequence fragments that are directly connected to characteristics of concern (i.e., those that confer or help to confer high levels of pathogenicity, infectivity, etc.), therefore limiting the database to sequences that bear a biosecurity risk. This would require an internationally curated, peer-reviewed database that is acceptable to both the community and authorities.

A first step in this direction is the Virulence Factor Information Repository (VIREP), in which sequence-based virulence factor information generated by screening programs can be shared and discussed.[102] Such a database could also provide the basis for the transition from an organism-centric perspective on biosecurity to a sequence- or gene-centric view, which is also an ongoing issue with regard to the above-mentioned control lists of hazardous biological agents, such as the Select Agents and Australia Group lists.[103] According to workshop participants, the further development of the sequence database is the single most security-relevant technical implementation issue for the industry.

In addition, keeping and sharing records within and between companies on sequences, associated virulence factor information, and customers causing positive hits could help to improve the effectiveness of the screening procedure and overcome some of the problems associated with false positive and false negative hits. In this regard, the industry-wide sharing of best practices, such as research undertaken to investigate hits, and of data from, and experiences made with, concrete incidents would be of advantage to all companies and seems to make economic sense.[104]

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102 www.virep.org/.

103 Cf. National Research Council. 2010. Sequence-Based Classification of Select Agents: A Brighter Line. http://dels.nas.edu/Report/Sequence-Based-Classification-Select-Agents/12970.

104 Cf. H. Bernauer et al. 2008. Technical solutions for biosecurity in synthetic biology. IASB workshop report.

Unsurprisingly, there are issues that arise when sharing information that might be sensitive or proprietary. An eventual capacity to detect orders split across different gene synthesis providers would require the cross-checking of orders (or checking them against a central, independent, trusted database). This would mean transmitting ordered sequence and customer data, which presents numerous privacy, contractual, and competitive concerns. While these challenges are not necessarily insurmountable, overcoming them would require a dedicated international effort.

The screening of customers against several government-maintained lists of proscribed persons and companies, such as, among others, the US Department of Treasury OFAC Specially Designated Nationals and Blocked Persons List (SDN)[105] or the HADDEX[106] list of the German Federal Office of Economics and Export Control (BAFA), is also performed with commercially available software tools, such as the Bridger Insight[107] application. These procedures are apparently less well standardized than sequence screening. The regulations in question are vague except concerning export to foreign entities, and the lists differ widely between nations.[108] Closer international collaboration and more standardized regulations would be highly desirable, according to industry representatives.

Another problem mainly faced by European (or Non-US) gene synthesis providers is the question of what to do when the screening produces a positive hit and how to inform authorities. Currently, there are no guidelines on the appropriate action to take within the EU, and no point of contact in the EU administration has been designated. In the US, the aforementioned "Screening Framework Guidance" by the HHS recommends contacting the local FBI WMD Coordinator, the CDC and APHIS Select Agent Regulatory Programs, or, for international orders, the Department of Commerce's Office of Export Enforcement, and provides phone numbers and e-mail addresses.[109]

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105 www.treas.gov/offices/enforcement/ofac/sdn/.

106 www.ausfuhrkontrolle.info/ausfuhrkontrolle/de/arbeitshilfen/haddex/index.html.

107 www.lexisnexis.com/risk/solutions/bridger-insight.aspx.

108 H. Bernauer et al. 2008. Technical solutions for biosecurity in synthetic biology. IASB workshop report.

109 US Department of Health and Human Services. 2010. Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA. www.phe.gov/Preparedness/legal/guidance/syndna/Documents/syndna-guidance.pdf.

Recommendations

- Encourage the adoption of a screening framework by all DNA synthesis providers and other relevant actors, and monitor developments in this area. Provide a suitable international forum for the harmonization of current efforts, the geographic expansion of screening practices, and the development of international standards and best practices. If needed, assess the feasibility and utility of mandatory screening of orders and customers (internationally).
- Support the screening initiatives of the DNA synthesis industry by providing them with regulatory and procedural guidelines and establishing a point of contact in government and law enforcement.
- Support the development of a seal of approval to certify compliance with existing best practices for screening DNA orders.
- Actively support the DNA synthesis industry in technical issues: Support the further development of an accurate sequence database; foster the transition from an organism-centric perspective on biosecurity to a sequence- or gene-centric view; work towards the inclusion of oligonucleotide orders in screening practices; encourage the industry-wide sharing of best practices and relevant order and customer information; standardize or provide support with international lists of proscribed persons and companies.

2.3. Code of Conduct Initiatives in Nanotechnology

In recent years, several code of conduct initiatives pertaining to nanotechnologies have been undertaken. Nanobiotechnology certainly falls within their purview, but none of them addresses the subfield explicitly, which should come as no surprise, given the diverse and dynamic nature of the nanotechnology field as well as the high level of uncertainty currently associated with it.

While nanomaterials are increasingly used in various consumer and industrial products, uncertainties exist with regard to the environmental and health impacts of nanoproducts and other associated risks; but also, as a result of these uncertainties, with regard to the lack of specific regulatory frameworks in most, if not all, countries.[110] The complexity of assessing associated risks and the diverse nature of nanotechnologies make it difficult to devise and implement domestic and international regulations. Currently, most governments generally apply existing provisions and endorse a precautionary strategy of risk control.

This creates a regulatory space where codes of conduct become increasingly important. In light of the lack of clear government regulations, codes of conduct provide industry and other actors with an initial, voluntary framework for addressing the environmental, health, and safety risks associated with nanotechnology. This situation is similar to the one DNA synthesis providers encountered a few years ago. They tried to overcome the regulatory vacuum by developing

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[110] Cf. D. M. Bowman and G. A. Hodge. 2008. 'Governing' nanotechnology without government? In: Science and Public Policy, 35(7), pp. 475–487.

their own rules and standards of best practice. Unlike in the case of the synthesis industry, however, code initiatives in the area of nanotechnology seem to be more government-driven, which may lead to a kind of hybrid approach between self-regulation and state-based models.[111]

Prominent examples of nanoscience and -technology code of conduct frameworks include the Code of Conduct for Responsible Nanosciences and Nanotechnologies Research of the European Commission (EC) and the Responsible NanoCode of the Nanotechnology Industries Association (NIA) in collaboration with the UK Royal Society and other partners, which are briefly discussed in more detail below. Other initiatives include the Principles for the Responsible Use of Nanomaterials of the German NanoKommission[112] and several code initiatives from the private sector, including BASF,[113] Bayer,[114] DuPont,[115] and the Swiss Retailers Association (IG DHS).[116]

2.3.1. European Commission Code of Conduct for the Nanosciences

In 2008, the European Commission (EC) published its "Recommendation on a Code of Conduct for Responsible Nanosciences and Nanotechnologies Research",[117] addressed to Member States of the European Union (EU). It aims at stimulating a debate between governments and stakeholders on the content and implementation of the Code and at guiding the formulation and implementation of a nanotechnology strategy in EU Member States through a set of principles and guidelines. EU Member States are urged to encourage the voluntary adoption of the Code by relevant stakeholders. To this end, the EU is also funding the "NanoCode" project under its current FP7 research support program with the

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[111] Ibid.

[112] Responsible Use of Nanotechnologies: Report and recommendations of the German Federal Government's NanoKommission for 2008. http://ec.europa.eu/health/ph_risk/documents/nanokommission.pdf.

[113] BASF Code of Conduct Nanotechnology. http://basf.com/group/corporate/en/function/conversions:/publish/content/sustainability/dialogue/in-dialogue-with-politics/nanotechnology/images/BASF_Code_of_Conduct_Nanotechnology.pdf.

[114] Bayer Code of Good Practice on the Production and On-Site-Use of Nanomaterials. www.sustainability2008.bayer.com/en/Bayer-Code-of-Good-Practice-on-the-Production-and-On-Site-Use-of-Nanomaterials.pdfx.

[115] Nano Risk Framework, in collaboration with the Environmental Defense Fund (EDF). http://nanoriskframework.com/.

[116] IG DHS Code of Conduct Nanotechnologies, 2008. www.igdhs.ch/m/mandanten/175/download/CoC_Nanotechnologien_final_16_01_09_e.pdf.

[117] http://ec.europa.eu/nanotechnology/pdf/nanocode-rec_pe0894c_en.pdf.

objective of developing a framework aimed at supporting the successful integration and implementation of the EU Code of Conduct.[118]

The EU Code places an emphasis on research activities in various institutional settings, including the private sector, but does not explicitly cover additional life-cycle stages of nanotechnology products, such as their production or disposal. The Code calls for responsible conduct in nanotechnology research and promotes seven principles towards this end: meaning (comprehensible to the public, respect for fundamental rights); sustainability (safe, ethical, and sustainable); precaution (application of the precautionary principle); inclusiveness (openness, transparency, and participation); excellence (best scientific standards); innovation (creativity and growth); and accountability (for social, environmental, and health impacts).

Security and dual-use issues are only marginally addressed in the EU Code, which mainly emphasizes precaution in dealing with potential safety, health, and environmental risks. Nevertheless, under the sustainability principle, stakeholders are urged only to undertake nanotechnology research activities that do “not harm or create a biological, physical or moral threat to people, animals, plants or the environment, at present or in the future.” While this statement was probably mainly formulated with health- and safety-related aspects in mind, the formulation allows for the enclosure of security considerations and would, for instance, “ban” research into nanotechnology-enhanced (bio-) weapons.

Furthermore, the Code contains guidelines on action to be taken based on the seven principles. Under the header “Prohibition, restrictions or limitations”, it states that “research funding bodies should not fund research in areas which could involve the violation of fundamental rights or fundamental ethical principles, at either the research or development stages (e.g. artificial viruses with pathogenic potentials).” This statement with the example in parentheses clearly covers the nano-enhanced development of hazardous bioagents, among other issues. However, it is puzzling to note that the statement reads “funding bodies should not fund research”, whereas the next statement on the enhancement of the human body begins with the words “research organizations should not undertake research”. This raises the question why the latter formulation using the term “research”, which would reasonably encompass and proscribe “funding” as well, was not used in the former statement.

Dual-use issues are also addressed in the guidelines to the Code. On the one hand, the statement that “competent authorities should evaluate the manner of applying ethical review requirements to dual-use nanotechnology research”

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[118] www.nanocode.eu/.

seems to be phrased in a way rather intended to avoid unnecessarily impeding beneficial research. On the other hand, the statement that stakeholders “are encouraged to consider […] the future implications of technologies or objects being researched” provides a vague reference to the desirability of assessing, among other possible implications, the potential for malevolent uses of (beneficial) research endeavors and outcomes.

To date, the EU Code has not been formally adopted in the private sector and has only been partially implemented in the Netherlands, where compliance with the Code is a mandatory condition for government funding.[119]

2.3.2. Responsible NanoCode

The Code of Conduct for Responsible Nanotechnology (“Responsible NanoCode”),[120] an initiative of the Nanotechnology Industries Association (NIA) in collaboration with the UK Royal Society and other partners, has been developed in dialogue with, and in parallel to, the work of the EC. The Responsible NanoCode also includes seven general principles intended to provide guidance on governance issues and establish good practices in the research, production, retail, and disposal of nanotechnology products. It is primarily targeted at governing bodies of relevant organizations and has been developed in a broad consultation process with European and international companies, scientists, governments, and NGOs. The Responsible NanoCode can be adopted by many different kinds of organizations, such as businesses, research laboratories, and universities, but clearly has a business-oriented focus. It aims at ensuring that nanotechnologies achieve their potential while promoting responsibility and accountability.

The seven principles of the Code are: board accountability; stakeholder involvement; worker health and safety; public health, safety, and environmental risks; wider social, environmental, health, and ethical implications and impacts; engaging with business partners; and transparency and disclosure. The seven principles are only qualified in a few sentences and intentionally left open for a detailed development by those using the code. Instead, concrete examples of good practices and suggestions for how an organization could implement the Code with respect to each of the seven principles are provided. There is no reference to the precautionary principle.

The Responsible NanoCode does not address any security or dual-use issues explicitly. Only Principle 4 “public health, safety and environmental risks” and

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[119] Synthesis report on codes of conduct, voluntary measures and practices towards a responsible development of N&N. Published under the NanoCode project, September 2010.

[120] www.responsiblenanocode.org/documents/TheResponsibleNanoCodeUpdateAnnoucement.pdf.

especially Principle 5 “wider social, environmental, health and ethical implications and impacts” leave undefined room for the inclusion and consideration of respective concerns. In the context of Principle 5, companies are encouraged to “consider what part they may play and how they may engage with others to develop appropriate responses to these important issues [wider social, environmental, health, and ethical impacts]”, which would also pertain to security and dual-use concerns.

Alongside the Code, a monitoring and benchmarking framework has been developed to evaluate companies’ activities and implementation of the Code. However, the framework has not been implemented so far due to a lack of financial resources and because it was felt that the time was not yet ripe, according to experts involved in the process. The Responsible NanoCode has not been formally adopted either yet by any company or other institutions, apparently due to legal liability issues, even though some members of the NIA use the Code as a basis for their operations.

2.3.3. Need for Explicit Dual-Use Messages

Security considerations are obviously not a particular focus of any of the nanotechnology code of conduct initiatives examined. Given the many uncertainties and various potential safety risks associated with nanotechnology as well as the implementation difficulties surrounding these initiatives, there are certainly many competing priorities, and it is legitimate to concentrate on other, possibly more pressing aspects than security. It might currently be premature and non-conducive to push for the inclusion of security considerations while stakeholders are already struggling to assess and find appropriate solutions to other open issues. From the point of view of the security community, however, the current vagueness with regard to security issues does little to address respective concerns and raise actors’ awareness of dual-use issues.

The opinions of project participants on the utility of a code of conduct for the nanosciences varied substantially. The majority of workshop participants felt that codes of conduct, best practices, and self-regulation could play an important role in raising the awareness of, and focus efforts on, dual-use issues. For instance, experts discussed options for governance of dual-use delivery devices, such as certain nanoparticles, developed for the targeted delivery of drugs that could be misused by a potential perpetrator to deliver a pathogenic or toxic bioagent more effectively (as discussed in the risk part of this report). Some experts suggested that in addition to the possibility of strengthening export control measures, security might be improved through a (voluntary) framework similar to the one in the DNA synthesis industry that, for example, stipulates the screening of customers and excludes delivery to home addresses.

One might argue that there is no need for a specific framework to address the security implications of nanobiotechnology, as the field is theoretically already covered by general initiatives in the life sciences or biotechnology. However, the problem here is that when a technology and its peculiarities are not specifically addressed, relevant actors do not necessarily feel concerned, especially if they do not regard themselves as life scientists or biologists. In order for such initiatives to be successful, experts felt, it is important that codes be tailored to the needs of relevant communities (in this case, to nanobiotechnology) so that the relevant actors do recognize the importance of looking into dual-use issues and ideally draft their own rules.

Experts recognized that there seems to be a general deficit of dual-use awareness in the nanosciences and called for greater education and awareness-raising efforts. The NSABB's considerations for the development of a code of conduct for dual-use research in the life sciences might be a good starting point for collaborative efforts to draft a code of conduct with a dual-use research focus for the field of nanobiotechnology and eventually nanotechnology in general.

Recommendations

- Foster the creation of a dual-use specific code of conduct and greater education and awareness-raising efforts in the nanosciences and –technologies.
- Promote and actively support the broad adoption of codes of conduct through information and outreach activities as well as with financial and political leverage.

3. International Arms Control: Existing Instruments and Potential Future Options

The ability to synthesize bioagents as well as the possibilities offered by nanotechnology to facilitate the development of effective bioweapons further complicate existing non-proliferation and export control efforts intended to constrain access to, and proliferation of, dangerous pathogens and relevant dual-use technologies. The implications of advances in bio- and nanotechnology for the development of new weapons as well as the consequences of the ability to engineer bioweapons as desired could pose a singular challenge to current arms control norms and instruments, in particular the Biological Weapons Convention (BWC).

Successfully addressing the security implications of progress in bio- and nanotechnology will require a mixture of bottom-up (communities engagement; self-governance) and top-down approaches (international arms control; laws and regulations) that provide protection for society against the unlawful and detrimental use of science and technology. While the previous sections mainly focused on community-based approaches, the following remarks provide ideas and thoughts on existing and potential future arms control mechanisms on the international level.

There is still much to do to shape and harmonize the national and international measures that regulate the fields of bio- and nanotechnology. Experts fear that the chaotic, uncontrolled development of bio- and nanotechnology may create catastrophic consequences for mankind. The international community (and countries actively engaged in the area) should initiate a process for establishing systematic national and international rules, control measures, and organizational structures that facilitate future developments in bio- and nanotechnology, while minimizing the chances of misuses by terrorists and certain state organizations.

3.1. Biological and Toxin Weapons Convention (BWC)

As implied in Article I of the BWC, which forbids states parties to develop, produce, stockpile, or otherwise acquire or retain "microbial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes",[121] the treaty applies to biological agents and toxins that were syn-

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[121] Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction. Emphasis added. www.unog.ch/80256EDD006B8954/(httpAssets)/C4048678A93B6934C1257188004848D0/$file/BWC-text-English.pdf.

thetically produced or modified. The view that all relevant scientific and technological advances in biotechnology are covered by the BWC has been reaffirmed in several Final Declarations of successive Review Conferences (RevCon), and the language used in these declarations provides coverage of developments in synthetic biology.

In the Final Declaration of the Second RevCon, States Parties reiterated that "the Convention unequivocally applies to all natural or artificially created microbial or other biological agents or toxins whatever their origin or method of production. Consequently, toxins [...] of a microbial, animal or vegetable nature and their synthetically produced analogues are covered."[122]

The same applies to nanotechnology. Although not explicitly mentioned, nanotechnology-enhanced bioweapons, such as the use of nanoparticles to deliver bioagents, would clearly violate the provisions set forth in the BWC. However, with respect to certain future possibilities offered by nanotechnology, such as microscopic biological-technical hybrid organisms that intervene in biological processes by imitating the effects of enzymes or toxins, it may be doubtful whether these are covered as well by the treaty due to the degree of artificiality. There have already been requests to clarify the scope of the BWC with regard to such issues.[123]

Scientific and technological developments relevant to the BWC have been addressed in a variety of media. In addition to official Convention documents, several background papers for meetings of the BWC, prepared by states parties or the BWC Implementation Support Unit (ISU), have examined relevant issues in synthetic biology and nanotechnology.[124] There have also been several side events in the framework of the BWC Intersessional Process that have specifically dealt with advances in synthetic biology and nanotechnology.[125] Such a high level of engagement is an indication of states parties' continuing interest

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[122] (Final Declaration of the Second BWC Review Conference. www.opbw.org/rev_cons/2rc/docs/final_dec/2RC_final_dec_E.pdf.

[123] Cf. Scientific and Technological Developments Relevant to the Biological Weapons Convention – submitted by the Netherlands, 2006. www.opbw.org/rev_cons/6rc/docs/adv/BWC.Conf.VI_S&T_neth_en.pdf. See also J. Altmann. 2005. Nanotechnology and Preventive Arms Control. DSF Forschung No. 3, Osnabrück: DSF.

[124] Cf., for instance, BWC/MSP/2009/INF.1 and BWC/MSP/2008/INF.1 Background Information on Scientific and Technological Developments that may be Relevant to the Convention - Submitted by the Implementation Support Unit; BWC/MSP/2008/WP.3 IASB Code of Conduct (Draft) - Submitted by Germany; BWC/MSP/2008/MX/WP.11 Oversight of Emerging Technologies: Examples of UK Approaches to Responsible Development of Science - Submitted by the United Kingdom; BWC/MSP/2008/MX/WP.4 Synthetic Biology: A Transforming Technology - Submitted by the United States of America; BWC/CONF.VI/INF.4 Background Information Document on New Scientific and Technological Developments Relevant to the Convention.

[125] Cf., for instance, BWC MX 2008 Synthetic Biology Seminar, www.unog.ch/unog/website/disarmament.nsf/(httpPages)/98DD55F8A0EF259DC12574B200461162?OpenDocument.

in these areas and suggests a certain level of awareness of potential problems.

The BWC lacks a compliance and verification mechanism. Work on a protocol to create a legally binding technology-based control regime started in 1992, but was stopped in 2001. As further elaborated below, some experts have proposed that it would be desirable to resume work on such a protocol, whereas others questioned the feasibility of such an endeavor.

3.2. Chemical Weapons Convention (CWC)

The CWC provides additional coverage for toxins that are already subject to the BWC. Article I prohibits the development, production, acquisition, stockpiling, retention, transfer, or use of chemical weapons and toxic chemicals and their precursors, respectively. Toxic chemicals are defined in Article II as "any chemical which through its chemical action on life processes can cause death, temporary incapacitation or permanent harm to humans or animals. This includes all such chemicals, regardless of their origin or of their method of production, and regardless of whether they are produced in facilities, in munitions or elsewhere."[126] Accordingly, synthetically produced toxins, and generally any chemical and precursor as defined by the Convention that is derived from engineered bacterial metabolic pathways clearly fall under the Convention, unless they are intended for peaceful purposes and their types and quantities are consistent with such purposes.

In addition, the CWC explicitly refers to agents that can be used against humans or animals, whereas there is no such qualification in the BWC, which more broadly refers to hostile use. Thus, while employing biological agents against plants is prohibited, this is not the case with chemical agents.

Nanotechnology-enhanced chemical and toxin weapons are also covered by the CWC, as long as the "chemical action on life processes" is given. The issue was raised as to whether this would also cover offensive nanotechnology-based supramolecular systems or nanomachines that would be functionally equivalent to chemical weapons but would act mechanically, electrically, or thermally to destroy cells or cell components.[127] Depending on how one defines "chemical action", such a notional weapon might likely be outside the scope of the CWC, which suggests the need for further clarification of the Convention's coverage. Additionally, the lists of toxic chemicals and precursors covered by the CWC have not been updated since the treaty entered into force in 1997.

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[126] Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction. Emphasis added. www.opcw.org/index.php?eID=dam_frontend_push&docID=6357.

[127] Cf. J. Altmann. 2005. Nanotechnology and Preventive Arms Control. DSF Forschung No. 3, Osnabrück: DSF.

In contrast to the BWC, a verification mechanism is included in the framework of the CWC, which is administered by the Organisation for the Prohibition of Chemical Weapons (OPCW). The OPCW conducts inspections of certain military and industrial plants and monitors chemical disarmament in all member states. The Convention also contains a mechanism, albeit thus far not exercised, to conduct a challenge inspection of a suspected violator. Many observers mention the CWC inspection and verification regime as a model for establishing similar structures in the framework of the BWC. However, many experts participating in this assessment noted that such a model would be fundamentally inappropriate in a biological setting.

3.3. Australia Group (AG)

The Australia Group (AG) is an informal arrangement that aims at minimizing exporting nations' risk of assisting chemical and biological weapons proliferation. While the group places no legal constraints on its members, a shared commitment to non-proliferation forms the basis for cooperation, information exchange, and the coordination of export control and licensing measures. All 41 group members are parties to both the CWC and the BWC; supporting these regimes is one of the main objectives of the AG's activities.

Following the 2007 AG plenary meeting, in which members agreed to pay particular attention to synthetic biological agents with a view to formulating an appropriate response, a synthetic biology advisory body was formed during the 2008 meeting "as a means of ensuring the Group is kept abreast of, and can respond quickly and appropriately to, technological developments in this area". In 2009, the AG reiterated its commitment and considered a report on synthetic biology from the advisory group, whose focus was broadened to include a range of evolving technologies. During the 2010 plenary, the Group "enhanced its vigilance with regard to the proliferation risk associated with new and emerging technologies" by "adopting specific recommendations from its technical advisory group".[128]

The AG maintains several control lists of chemicals, biological agents, and toxins as well as dual-use equipment and technologies that are constantly updated in response to technological advances and related concerns. The AG's List of Biological Agents for Export Control[129] covers not only bioagents per se, but also "genetic elements that contain nucleic acid sequences associated with

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[128] Cf. www.australiagroup.net/en/agm_june2007.html; www.australiagroup.net/en/agm_apr2008.html; www.australiagroup.net/en/agm_sept2009.html; and www.australiagroup.net/en/agm_june2010.html.

[129] www.australiagroup.net/en/biological_agents.html.

the pathogenicity of any of the microorganisms in the list" as well as "genetic elements that contain nucleic acid sequences coding for any of the toxins in the list, or for their subunits". Genetic elements include, among others, "chromosomes, genomes, plasmids, transposons, and vectors whether genetically modified or unmodified", which also encompasses viroids and certain other RNA constructs, according to experts familiar with the matter. Nucleic acid sequences are defined by the AG as "any sequence specific to the relevant listed micro-organism that in itself or through its transcribed or translated products represents a significant hazard to human, animal or plant health; or that is known to enhance the ability of a listed microorganism, or any other organism into which it may be inserted or otherwise integrated, to cause serious harm to human, animal or plant health".

In accordance with these definitions, synthetic genes and genomes associated with the pathogenicity or toxicity of listed bioagents are covered by the AG's export control arrangement. However, as confirmed by a country representative to the AG, "genetic elements" as defined above refers to nucleic acid-based elements that are either able to replicate or to transpose. Accordingly, the control list only covers the export of double-stranded DNA constructs and theoretically of certain RNA oligonucleotides,[130] but not of synthetic DNA oligonucleotides, which could be assembled into a functioning bioagent on the control list. Therefore, providers of synthetic oligonucleotides and their customers do not have to meet any export control requirements under the AG's provisions.

The reasoning is much the same as in the case of oligonucleotide orders, which are not screened against pathogenic sequences by synthesis providers (see the section on screening frameworks above) - mainly technical (i.e., too many false positive hits) and organizational problems (i.e., the lack of information exchange mechanisms between providers on customers and short sequences ordered). This situation provides potential perpetrators with a loophole for acquiring components that could be built into a controlled bioagent. Should advances in screening techniques provide the ability to overcome the technical hurdles, it would be desirable to update the respective national and international trade regulations, including the AG's control lists.

The AG Control List of Dual-use Biological Equipment[131] does not specifically include synthesis technologies and materials, such as DNA synthesizers and sequencers or key precursors. Including such items would not make much sense, as such tools are readily available worldwide at low prices. Nevertheless,

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[130] Such as the Potato Spindle Tuber Viroid, which can be found on the AG plant pathogens control list.

[131] www.australiagroup.net/en/dual_biological.html.

the AG Guidelines[132] contain a "catch-all" clause, in which member states are requested to include in their export regulations the requirement of "an authorisation for the transfer of non-listed items [... if] it is established that the items in question may be intended, in their entirety or part, for use in connection with chemical or biological weapons activities".

Concerning nanobiotechnology and certain nanoparticles that could be misused for biological and chemical weapons development, experts familiar with the AG's deliberations confirmed that nanotechnology in general is a topic that is being discussed in the framework of the AG, but no official policy has been formulated, and no respective control lists currently exist.

3.4. Implications and Future Options for Biotechnology

All potential bioweapons-related applications of synthetic biology and nanobiotechnology discussed in this report would be covered by the BWC, and to some extent, by the CWC. They are, therefore, inconsistent with international law. There are, however, only few actual mechanisms for controlling the proliferation of relevant technologies and knowledge, apart from the activities of the AG. However, the AG is a voluntary arrangement, has a comparatively small membership, and cannot provide comprehensive coverage. It has also been described as lagging behind certain technology trends.[133] Experts generally felt that the international community is inadequately prepared for addressing the various challenges highlighted in this report.

In light of these shortcomings, some project participants suggested the best way forward would be to resume work on a compliance and verification mechanism and create a dedicated international organization, in the framework of the BWC, to cope with the task. A reliable verification framework, it is argued, would act as a deterrent when a state considers whether it should violate or circumvent its treaty obligations or an international norm. It would also reinforce national efforts to detect and interdict similar activities by groups or organizations. Arrangements in place to address other weapons categories, such as the OPCW in the context of chemical weapons or the International Atomic Energy Agency's (IAEA) safeguards systems for nuclear weapons, are often referenced as models for establishing similar structures in the context of the BWC.

However, apart from numerous implementation difficulties and shortcomings that both organizations are facing, the majority of experts sounded a note

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[132] www.australiagroup.net/en/guidelines.html.

[133] R. Weller et al. 2006. Synthetic Biology: Recommendations to Manage the Growing Proliferation Threat. Pacific Northwest National Laboratory.

of caution regarding the peculiarities and distinct nature of the biosciences. The technology involved and its implications are quite distinct from the nuclear or chemical weapons fields, due to the comprehensive dual-use nature of biotechnology and the ability of bioagents to replicate.

Nuclear non-proliferation efforts are facilitated by several factors. Nuclear power or weapons activities are mostly pursued by state bodies and extensively regulated, and they require large and highly visible facilities and substantial supplies of dangerous materials and expensive equipment that do not have multiple uses or whose civilian applications are limited. Relevant activities, technologies, and materials are broadly controlled by the IAEA and well-established export control regimes, which make it nearly impossible to build up respective capabilities or transfer nuclear-related components undetected.[134]

The situation with biology is almost the opposite. The nature of progress in biotechnology profoundly complicates efforts to control the technology and its proliferation. Neither is there an international monitoring body, nor are there any effective and verifiable export control and non-proliferation regimes in place. Even if it should prove possible to develop such mechanisms, they would likely be less effective than those in the nuclear field.

It is generally difficult to identify bioweapons-related activities and materials, as exactly the same activities and substances are used for peaceful purposes. Relevant research could be carried out in small civilian and commercial laboratories of which there are tens or even hundreds of thousands around the globe. The sheer number of biotechnology facilities that would have to be controlled, for instance, makes any reasonable inspection regime a very tough, if not impossible, venture. Furthermore, weapons-related activities could relatively easily be concealed behind legitimate peaceful activities – providing a latent breakout capacity.

In addition, expertise, materials, and equipment are used across many life science disciplines and are already available to varying degrees around the globe. The proliferation of knowledge, materials, and equipment in biotechnology, albeit not specifically weapons-related, has already taken place, according to experts. It is very likely that relevant expertise and equipment will continue to spread to new geographical locations and societal sectors, especially if synthetic biology succeeds in making biology an engineering discipline and accordingly more accessible. The costs of constraining commercial and academic access to materials and technology in biology would be daunting, not only because of the tremendous resources required to establish an effective verification regime, but

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[134] Ibid.

also in societal and political terms as well as with regard to the consequences of impeding beneficial research.

It is important to build networks of actors and checks as part of a web of activities to address the challenges posed by modern biology. While these networks surely need to be closely tied to a national and international legal and regulatory framework, most experts stressed that the verification of arms control in bio- and probably also nanotechnology might, at present, not be politically or technically feasible.

The BWC has well-known shortcomings and should certainly be strengthened in various ways. All the experts involved in this project agreed that an international verification mechanism would ultimately be desirable. However, many experts felt that a technology-based control regime built upon current capabilities could not provide the same level of oversight and assurance as in the chemical and nuclear weapons fields. In light of the biotechnological advances that can be expected over the coming decades, and the potential for misuse associated with them, most experts are also convinced that, even if agreement on such a protocol should become politically feasible, it would be a significant technological challenge, if not impossible. Due to the nature and diffusion of biotechnology, experts felt that any effort to pursue such a solution would likely dwarf parallel efforts in the chemical and nuclear weapons fields, in terms of the efforts needed and the challenges to be overcome.

Nonetheless, experts recognized that bottom-up approaches such as community action and engagement alone are insufficient. Experts agreed that traditional arms control, and in particular the BWC, would continue to play an important role in a networked approach, as propagated in this report, but that it would be quite different from respective efforts in the nuclear or chemical areas. Most experts felt that the main role of such instruments in the bioweapons field continues to consist of setting norms and taboos rather than verifying compliance with obligations.

However, there must also be a sensible legal and regulatory framework to enable the interdiction of those that are intent on acquiring and using biological weapons and to punish them appropriately. At the national level, this requires an updated regulatory framework and a closer working relationship between law enforcement and science. At the international level, there is much room and necessity for further development and the buildup of an international capacity to address the challenges. Many experts noted that the international community needs new and innovative governance strategies, which must rely on a network of various prevention and detection efforts; that it must make use of multiple intervention points, on different intervention levels; and that it needs to go significantly beyond “traditional” arms control.

One such idea identified by experts is the establishment of an international authority, perhaps equipped with a UN mandate, to work with states, industry, academia, and other stakeholders on relevant issues. Such an agency would not provide legally binding arms control mechanisms or compliance assurances. Instead, among other responsibilities, it would – in close collaboration with states and stakeholders – work on issues such as outreach, education, and awareness-raising; monitor developments in science and technology; promote good practices in biosafety and biosecurity; provide regulatory advice; work on the international harmonization and universalization of measures, and would coordinate and promote the international portfolio of respective efforts.

3.5. Implications and Future Options for Nanotechnology

Even though the project focused on bioweapons and specific related aspects of nanotechnology, the broader issue of how to address the security implications of nanotechnology repeatedly arose during the workshops. According to experts, the matter seems to be more closely related to biotechnology than to nuclear technology, as the field of nanotechnology must also come to terms with an extensive dual-use problem.[135]

Dangerous materials and techniques cannot be clearly identified, due to their diverse nature and dual-use potential; research and development activities do not require huge and therefore visible resources; and activities in this field are pursued around the globe and not limited to a few countries. In addition, the field of nanotechnology encompasses such a diverse range of methods and materials that blend into other disciplines that the boundaries become blurred and no single area or technique could be identified as the major area of concern. This makes devising and implementing domestic and international regulations, let alone the establishment of an arms control regime, significantly more complicated.[136]

Many advances in nanotechnology that could potentially contribute to the development of new kinds of nano-enabled weapons and military equipment – other than those related to existing arms categories, such as biological or chemical weapons – are currently not covered by any international arms control regime. This led a few project participants to stress the need for an international authority that would install a safeguard system to monitor and control

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[135] See M.E. Kosal. 2004. Is Small Scary? Nanotechnology Research in an Age of Terrorism. In: Bulletin of the Atomic Scientists, Vol. 60, No. 5, pp. 38-47.

[136] Cf. M. E. Kosal. 2009. Nanotechnology for Chemical and Biological Defense. Springer Academic: New York.

weapons-related developments in nanotechnology, which would require the negotiation of a new type of treaty regime, backed up by a new international organization.

As a means of preventing existential threats, one expert even suggested that the challenges ahead imply a need for fundamental change in the international system and in the way security is provided within and between states, namely, by creating a monopoly of legitimate violence (e.g., resting with a democratized UN) while reducing national sovereignty in relevant areas. These issues were not comprehensively addressed during the workshops; however, most experts agreed that the daunting challenges of establishing an international nanotechnologies regime are probably greater than those faced in the biological weapons field, and that the technical and political feasibility of such an endeavor is highly doubtful.

As an alternative to the negotiation of a new convention that would cover nanotechnology-based weapons systems, experts also suggested pragmatically adapting the CWC and BWC to include certain artificial microscopic systems that mimic chemical or biological action on cells or organisms, as briefly elaborated above. However, this would not cover all the possible weapons applications that nanotechnology might enable, many of which are completely removed from the sphere of the life sciences, such as kinetic weapons.

Another concept briefly discussed during the response workshop is that of preventive arms control. This approach aims at limiting the risk of new technologies being misused for military purposes and has been specifically applied to nanotechnology.[137] The basic concept of preventive arms control is that militarily usable technology or weapons systems should be banned before they can be developed, tested, or acquired. In order to identify and ultimately limit problematic technology developments, a number of successive steps are envisaged: prospective analysis of the technology and its potential military uses; an evaluation of problematic military technology applications under several criteria; and the design of possible limits and verification methods. In order to identify and evaluate military-relevant technologies that may entail special dangers and the fields where preventive limits should be applied, three groups of criteria should be assessed: threats to arms control agreements and the international law of warfare; threats to stability (in terms of a first-strike capability, the likelihood of instigating an arms race, and proliferation concerns); and threats to humans, the environment, or society. Afterwards, nations would ideally start negotiating a corresponding agreement, which would include a verification mechanism,

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[137] Cf. J. Altmann. 2006. Military Nanotechnology: Potential Applications and Preventive Arms Control. Abingdon/New York: Routledge. And, J. Altmann. 2005. Nanotechnology and Preventive Arms Control. DSF Forschung No. 3, Osnabrück: DSF.

or update existing agreements, such as the BWC, to include nanotechnology-related aspects.

Potential limits would have to be evaluated against the level of threat that a particular technological application poses, its potential positive uses (and the respective implications of a ban), and the feasibility of verification. Because of the wide variety of nanotechnologies, no single treaty is proposed; rather, specific limits concerning the most problematic military applications are recommended that could be embedded in the general arms control and disarmament framework. According to the authors of the concept, those applications that pertain to biotechnology or bio-weapons include: non-medical body implants and other body manipulations; mobile, (partly) artificial systems below a certain size (i.e., mini-/micro-robots); and new biological and chemical weapons that are enabled by nanotechnology.[138] This was not a specific topic of discussion during the workshop, however.

Recommendations

- Consider ways and needs for establishing systematic national and international legal and regulatory frameworks to address the security implications of progress in bio- and nanotechnology.
- Work with various stakeholders towards initiating a process to develop a web of innovative measures as well as organizational structures beyond traditional arms control that could help reduce the misuse of progress in bio- and nanotechnology.
- Strengthen the links between the science and security communities; identify areas of shared interest and projects that offer mutual benefits.
- Uphold and strengthen the norms of the BWC and the CWC and clarify the provisions set forth in both Conventions to provide clear coverage of synthetic biology and relevant nanotechnology developments.
- Support and strengthen the BWC Implementation Support Unit (ISU).
- Support and engage with the AG to ensure that their efforts address relevant developments in synthetic biology and nanotechnology to the fullest extent possible.
- Reinforce efforts to continuously monitor science and technology developments in bio- and nanotechnology in order to identify areas with misuse potential and to strengthen efforts to address such threats.
- Work towards an international consensus on how to address the future international security implications of nanotechnology. To this end, foster the promotion of good practices, reinforce the international portfolio of respective efforts, and support the elaboration of a joint evaluation methodology in nanosafety and -security on a voluntary basis.

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[138] Ibid.

4. Technological Potential for Countermeasures

Synthetic biology and nanotechnology offer an array of possibilities for new countermeasures against deliberately released and naturally occurring pathogens. Consequently, experts emphasized that any strategy to mitigate the risks posed by biology, including those posed by synthetic biology and nanobiotechnology, should also take into consideration and foster the potential defensive, protective, and preventive applications of the two emerging technology fields.

4.1. Synthetic Biology for Biological Defense[139]

Although not discussed at great length at the workshop, experts acknowledged that synthetic biology offers the possibility of new countermeasures against the hostile use of biology, as well as against naturally occurring pathogens. Much of this potential stems from the increased speed and flexibility afforded by synthetic biology techniques to design and construct novel living systems, which, in turn, could be used to facilitate the production of next-generation systems for environmental detection, medical diagnostics, prophylactics, and therapeutics.[140] "Over the long term", as Mukunda et al. have pointed out, "DNA synthesis and synthetic biology may strengthen defensive capabilities against biological attacks and responses to natural epidemics, as the methods of synthetic biology permit [...] rapid analysis of natural and artificial agents, accelerated design of vaccines and pharmaceuticals, and faster mass production of pharmaceuticals."[141]

4.1.1. Detection and Surveillance

As a first line of defense, synthetic biology could play an important role in enhancing environmental detection of potential threat agents. Environmental detection (or surveillance) is an essential countermeasure for rapidly detecting whether there has been a biological attack and identifying the disease-causing agent for the purposes of employing medical therapeutics to mitigate the severity of the attack. Successful detection requires "sensitive, specific chemical or biological probes capable of discriminating true pathogens among a background of related microorganisms."[142]

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[139] This section was contributed to the report by R. Alexander Hamilton, Researcher, London School of Economics and Political Science (LSE), Department of Sociology, BIOS Centre, London, UK.

[140] Petro J.B., Plasse T.R. and McNulty J.A. 2003. Biotechnology: Impact on Biological Warfare and Biodefense. In: Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science, Vol. 1, No. 3.

[141] Mukunda G., Oye K.A. and Mohr S.C. 2009. What rough beast? Synthetic biology, uncertainty, and the future of biosecurity. In: Politics & Life Sciences. Vol. 28, No. 2, p. 20.

[142] Ibid., p. 12.

Present detection devices, which are often used to monitor municipal air and water supplies, take advantage of the human immune response to identify known pathogens of concern. Although a valuable contribution to biodefense, future detectors will not only need to respond to known pathogens, but also to unknown pathogens, whether they be genetically engineered for use in an act of bioterrorism or naturally occurring in the form of a new epidemic/pandemic influenza virus.[143] Synthetic biology techniques may someday provide “much faster responses [to pathogen detection] by engineering libraries of modified antibodies”, which could, in turn, be linked to “versatile and inexpensive cell-based signal output devices” that indicate the presence of a disease-causing agent.[144] Preliminary advances, including the development of an arsenic sensor proposed by a student team at the Genetically Engineered Machines competition (iGEM), offer an early indication of synthetic biology’s potential to contribute to this area.

4.1.2. Pre- and Post-Exposure Prophylaxis and Therapy

Synthetic biology techniques may become valuable tools in the development and production of pre- and post-exposure prophylaxis in the event of a deliberate attack involving a known or an unknown pathogen. Some of the greatest gains to be realized in this area stem from the potential of synthetic biology to facilitate the rapid design and production of agent-specific vaccines and antibiotics. With regard to vaccine research, Wimmer et al. note that the “chemical synthesis of viral genomes provides a new and powerful tool for studying the function and expression of viral genes, as well as their pathogenic potential.”[145]

Furthermore, the potential of synthetic biology techniques to introduce large-scale changes into numerous virus strains, as a way of decreasing the lag time in developing vaccines in response to a broad variety of agents is highlighted, including those for which there exists no natural template.[146]

Equally, synthetic biology might be applied in the production of antibiotics against bacteria that are unresponsive to existing treatments. “If a new type of organism were to be identified for which no available antibiotic is effective, metabolic engineering via synthetic biology techniques might shorten the period

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[143] Petro J.B., Plasse T.R. and McNulty J.A. 2003. Biotechnology: Impact on Biological Warfare and Biodefense. In: Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science, Vol. 1, No. 3.

[144] Mukunda G., Oye K.A. and Mohr S.C. 2009. What rough beast? Synthetic biology, uncertainty, and the future of biosecurity. In: Politics & Life Sciences. Vol. 28, No. 2, p. 12.

[145] Wimmer E., Mueller S., Tumpey M.T. and Taubenberger J.K. 2009. Synthetic viruses: a new opportunity to understand and prevent viral disease. In: Nature Biotechnology, Vol. 27, No. 10, p. 1163.

[146] Ibid.

necessary to develop a new therapy for it."[147] Furthermore, these techniques could also be deployed preemptively, "developing a repertoire of novel antibiotics, some of which could be held in reserve" in anticipation of future attacks.[148] The development of anticipatory protection and defense strategies, however, blends into offensive research and could, especially if done in secrecy, raise suspicion about military preparations.

4.1.3. Attribution

Synthetic biology may also come to play an important role in helping to identify the origin of an agent used in a bioterrorist attack. As was the case with the 2001 anthrax letter attacks, one critical step in identifying the perpetrator(s) of the attack consists of successfully attributing an agent to the laboratory in which it has been produced.

Current methods of attribution require comparing genetic polymorphisms against a database of different strains and isolates from the environment and laboratories around the world. Given the numerous strains of viral and bacterial agents worldwide, this can clearly be a complicated and time-consuming task that may interfere with the progress of an investigation. Moreover, a novel pathogen might be unrecognizable to investigators, as it would not match any known pathogenic sequence, which calls for improved methods of attribution. In the future, incorporating software into DNA synthesizers that tags products with a signature sequence might provide a further means of attribution of agents derived from synthetic DNA.[149]

4.1.4. Novel Capabilities

More imaginative countermeasures that could be facilitated by synthetic biology might include entirely new defensive capabilities and therapies. In the long term, bacteriophages could be designed that specifically attack engineered pathogens; or bacterial cells could be produced that target tumors and kill cancer cells by injecting toxins. Often referred to as "blue skies" possibilities, there are numerous applications for synthetic biology to defend against disease and disease causing agents. Synthetic viral genomics, for example, offers the possibility of producing "redesigned particles that can provide new insights into

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147 Mukunda G., Oye K.A., and Mohr S.C. 2009. What rough beast? Synthetic biology, uncertainty, and the future of biosecurity. In: Politics & Life Sciences. Vol. 28, No. 2, p. 13.

148 Ibid.

149 Cf. Petro J.B., Plasse T.R. and McNulty J.A. 2003. Biotechnology: Impact on Biological Warfare and Biodefense. In: Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science, Vol. 1, No. 3.

biology or the design of new vectors that can prevent or cure infectious diseases [or] cure genetic deficiencies."[150]

Looking further into the future, as well as thinking "out of the box", Aldrich et al. propose a scenario that depicts the tools and know-how for genome engineering and design as being widely diffused – where dozens of commercial gene foundries operate around the world and bench-scale gene synthesis tools are commonly available – allowing amateur biologists and university-level researchers to play an unauthorized, though possibly beneficial role in countering biological threats.

In this scenario, the authors suggest, such a community might respond to a pandemic influenza by drawing on published information describing the DNA vaccine in an effort to produce its own vaccine that is then sold on the grey market, increasing scarce vaccine supplies.[151] However, such a scenario could also open up possibilities for exactly the kind of hazardous or malicious activity that it is supposed to act against; e.g., an untested grey-market vaccine could have many dangerous side effects.

4.2. Nanotechnology for Biological Defense[152]

Nanotechnology has emerged as scientific and technology route that, like biotechnology, carries the potential for groundbreaking applications in particular for defensive countermeasures against biological weapons. Both fields hold great promise for development of new protective capabilities. Nanotechnology, encompassing a broad spectrum of nanoscale science and engineering, can be described as an array of fundamental knowledge and enabling technologies resulting from efforts to understand and control the properties and function of matter at the nanoscale.[153]

The world is probably 20 years away from witnessing the full impact of nanotechnology on defensive capabilities. Now is therefore the time to explore the potential for new science and new breakthroughs, and now is the time to

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[150] Wimmer E., Mueller S., Tumpey M.T. and Taubenberger J.K. 2009. Synthetic viruses: a new opportunity to understand and prevent viral disease. In: Nature Biotechnology, Vol. 27, No. 10, p. 1163.

[151] Aldrich S., Newcomb J., Carlson R. 2008. Scenarios for the future of synthetic biology. In: Industrial Biotechnology, Vol. 4, No. 1, pp. 39-49.

[152] This section was contributed to the report by Margaret E. Kosal, PhD, Center for International Strategy, Technology, and Policy (CISTP), Sam Nunn School of International Affairs, Georgia Institute of Technology, Atlanta, USA.

[153] National Research Council. 2006. A Matter of Size: Triennial Review of the National Nanotechnology Initiative. National Academies Press: Washington, D.C.

begin the strategic thinking needed to achieve, exploit, and defend against these discoveries.

Over the last ten years, a significant share of the resources for biological defense have been focused on near-term goals in development, acquisition, and deployment of detection, protection, decontamination, and medical countermeasures. While exploiting "low-hanging fruits" and using non-developmental items and commercial off-the-shelf technologies may satisfy immediate goals, it is unlikely to be adequate for addressing an evolving threat or providing revolutionary capabilities.

A comprehensive strategy would be to balance more revolutionary approaches with the focus on near-term solutions and evolutionary improvements to currently deployed systems. The rapidly evolving nature of technology requires the defense communities to innovate so as to remain ahead of adversaries.[154] Implementation of such a strategy begins with recognition of the need to leap ahead and embrace truly farsighted concepts while fostering integrated, multidisciplinary, and cross-cutting basic research approaches.

Such an analysis and strategic plan for nanotechnology for defense against biological threats and for the development of biological countermeasures was detailed extensively in the 2009 publication, Nanotechnology for Chemical and Biological Defense.[155] Many of the ideas mentioned here (as well as others) are expanded and detailed in that work.

4.2.1. Inherent Interdisciplinarity

Defense against chemical or biological weapons necessarily involves the physical sciences, the life sciences, the medical sciences, and several engineering communities. Narrow demarcations of research into traditional disciplines – literally "old-school thinking" – have become increasingly less likely to yield transformational technologies. Nanotechnology has emerged as an intrinsically interdisciplinary domain with the potential to bridge many disciplines. Notable examples are found in the design of sensors that use active complexes that bind DNA to carbon nanotubes; this was a joint effort of electrical engineers and computer scientists[156] in one case and originated in a physics and astronomy

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[154] Department of Defense. 2007. Technological Change and the Future of War. Defense Science Board Summer Study, Washington, D.C.

[155] M. E. Kosal. 2009. Nanotechnology for Chemical and Biological Defense. Springer Academic: New York. www.springer.com/materials/nanotechnology/book/978-1-4419-0061-6.

[156] C. Dwyer, et al. 2002. DNA Functionalized Single-walled Carbon Nanotubes. In: Nanotechnology, Vol. 13, pp. 601-604.

department research group in another.[157]

Nanotechnology and biotechnology enjoy a great deal of overlap in many research laboratories. A current focus of research in this cross-cutting area is on using genetically engineered viruses, proteins, DNA, and other biological moieties as templates for assembling nanostructures and understanding structure-function biological interactions. For example, by combining a genetically engineered protein with nanoscale particles, researchers have created a new kind of solar cell.[158]

Today, there are already substantial overlaps between the medical and physical, chemical, and biological defense research communities. For example, genetics research has long been incorporated into detection schemes in industrial pharmaceutical and medical device development. In some applied research and advanced development efforts, however, isolated islands of specialization remain; for example, animal testing to satisfy regulatory requirements. The benefits of improved coordination among large cross-cutting programs in both reduced cost and increased output has become very clear. Narrow demarcations of research into traditional divisions are less and less likely to yield the strategies and results needed to deliver biological weapons countermeasures today and for the future.

4.2.2. Detection and Diagnostics of Biological Agents

Nano-enabled technologies offer some inherent advantages for biological agent detection and diagnostics at all levels. Foremost, the innovative properties of nanostructures can be exploited for the transduction of agent reaction into a discernable signal. Instrumentation developed to maximize signal with minimal noise via nanotechnology may provide new ways for detection and discrimination of biological threat agents. Furthermore, miniaturization beyond microelectronics and micro-electromechanical systems (MEMS) may facilitate the development of array detectors that provide expanded functionality per unit volume.

Miniaturization, while sure to degrade the state-of-the-art capability found in a full-scale instrument, will also allow combinations of instruments utilizing small volumes and little electrical power. The nanoscale will enable the continuation of microtechnology advances, and the “lab-on-a-chip” concept can be realized. Small-scale array detection based on microfluidics principles may also

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157 C. Staii, M. Chen, A. Gelperin, & A.T. Johnson. 2005. DNA-decorated Carbon Nanotubes for Chemical Sensing. In: Nanotechnology Letters, Vol. 5, pp. 1774-1778.

158 S. Y. Ding, et al. 2003. Quantum Dot Molecules Assembled with Genetically Engineered Proteins. In: Nanotechnology Letters, Vol. 3, pp. 1581-1585.

provide the opportunity for integrating chemical and biological detection and diagnostics into the same systems.[159]

Detecting the presence of a chemical or biological agent and identification of exposed individuals is a complex challenge. Detection with the aim of warning individuals within a few minutes after an agent is dispersed allows action to minimize exposure. Detection with the intent to identify a treatment adds levels of complexity, with the need to identify specific agents, concentration levels, and the extent of exposure. Nanostructures can enhance detection to warn capabilities by augmenting sensitivity levels for gas phase detection and, potentially, by monitoring living systems, such as surrogate cell lines, for physiological distress.

The ability to detect very low concentrations of agents will always be desirable, if for no other reason than to ensure that long-term exposure in a previously contaminated environment will not have consequences. Nanoscale sensors have been demonstrated to be able to detect single moieties; but, thus far, only when those moieties can be delivered to a very small detection volume.[160] The collection and concentration of an agent is an important step in the detection process. Nanostructured materials will provide essential degrees of freedom in the construction of concentrators. The nanostructure high surface area and attendant surface modification and speed of access through interconnected porosity should enable the delivery of a highly concentrated sample of material from the concentrator into the detection volume. Examples of a potential combination of bio- and nanodevices include tamper-resistant, self-powered, smart nanoscale tags that can serve as sensors.

Current approaches to detection and diagnostics of biological agents are based on threat agent identification using agent-specific DNA sequences, antigen-antibody interactions, or analysis of biological activity. To reduce their size, these DNA sequences can be hybridized and antibodies or bioactive enzymes can be tethered to nanomaterials, such as carbon nanotubes or gold, silver, or silica nanoparticles. In many cases, nanomaterials themselves are either nonresponsive or non-specific to chemicals or biochemicals. In order to develop a sensing element, additional basic and applied research efforts in understanding and designing surface functionalization for molecular recognition are essential in the near term.[161]

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159 H. Craighead. 2006. Future lab-on-a-chip technologies for interrogating individual molecules. In: Nature, Vol. 442, pp. 387-393.

160 Y. Fang, et al. 2007. Electrical Detection of Single DNA Molecules with Silicon Nanowire Devices. In: Biophysical Journal, pp. 551A-560A.

161 Carbon nanotubes coated with single-stranded DNA (ssDNA), for example, have been tuned to sense different vapors such as methanol, dimethylmethylphosphonate, and dinitrotoluene by choosing the appropriate ssDNA base sequence (cf. A. T. Johnson, et al. 2006. DNA-decorated carbon nanotubes for Sensing. In: Physica Status Solidi B-Basic Solid State Physics, Vol. 243, pp. 3252-3256.). Polymer-nanomaterial composites constitute yet another way of functionalizing nanomaterials for selective detection.

Current program objectives for the detection and diagnostics of biological agents involve a variety of new technologies ranging from miniaturization of existing technology to entirely new detection schemes. Miniaturization will increase portability for field use and reduce the overall logistics burden. Further size reductions will increase the sensors that can fit into a small device as well. New technologies for the detection of biological agents at distances of tens to hundreds of meters are of great interest. New methods and instrumentation to reduce the incidence of false positive and false negative results are needed, and ideal systems will also increase the speed and sensitivity of the analysis.

With the miniaturization enabled by the use of nanostructures and lab-on-a-chip technologies, detection or identification devices may easily fit onto small unmanned aerial vehicles (UAVs). A suspicious cloud could be probed by flying the UAV through it or collecting physical samples from the site. The same miniaturization may enable small, low-power and easy-to-obscure unattended ground stations that could serve as remote site detection or identification stations. One example of miniaturization is that of flexible nanowire sensor arrays "printed" on plastic or polymeric substrates that may be wearable.[162] Another example for the specific detection of genetic material is the metallization of single strands of DNA, which allows them to conduct electricity. Based on self-assembled nanoscale circuits – using silver nanowires[163] or bimetallic nanowires[164] – the detection of biological agents is accomplished through DNA recognition.

4.2.3. Decontamination

Effective decontamination of military personnel, first responders, exposed civilians, equipment, and infrastructure remains a technical and practical challenge. While avoiding contamination is a first priority, it is not always possible. Tools are needed to neutralize hazards after biological threats have been deployed. Technologies such as sprays, mists, and dispersion methods, coatings and catalysts, and various types of washing and physical removal will be appropriate for different decontamination operations. Decontamination science and technology is targeted to carry out this mission while minimizing damage or degradation to the people, environments, and equipment involved. Technologies should therefore be noncorrosive and environmentally safe.

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[162] Silicon nanowires are formed using the superlattice nanowire pattern transfer (SNAP) deposition technique on silicon-on-insulator wafers. Cf. M.C. McAlpine, H. Ahmad, D. Wang, & J.R. Heath. 2007. Highly Ordered Nanowire Arrays on Plastic Substrates for Ultrasensitive Flexible Chemical Sensors. In: Nature Materials, Vol. 6, pp. 379-384.

[163] Erez Braun, et al. 1998. DNA-templated Assembly and Electrode Attachment of a Conducting Silver Wire. In: Nature, Vol. 391, pp. 775-778.

[164] M. Fischler, et al. 2007. Formation of Bimetallic Ag-Au Nanowires by Metallization of Artificial DNA Duplexes. In: Small, Vol. 3, pp. 1049-1055.

Another fundamental research area aims to produce faster and more accurate methods to predict and understand the physiological response to traditional and emerging agents, including low-level toxicology effects. In the civilian sphere, more accurate information is needed regarding toxic loads and reliable concentration data for acute and long-term exposures of the general population.

The opportunities for preparing a multipurpose catalytic material for decontamination, protection, and remediation of contaminated sites are very promising. By combining catalytic sites with light absorption, photocatalysts are produced. Using nanostructures for these photocatalysts generates several advantages for compounds that may otherwise be unstable in the air. A range of engineered semiconducting metal oxides and transition-metal oxygen-anion clusters (polyoxometalates or "POMs") catalyze photochemical and electrochemical decontamination by providing new mechanisms to reach the more stable decontaminated forms via processes with lower activation energies.[165] Many nanostructural possibilities for creating very effective nanomaterials for photocatalytic decontamination have been developed.[166]

A longer-term goal is to design nanomaterials that can select, detect, and decontaminate a wide range of agents. Hybrid materials combining organic and inorganic nanoparticles will be needed. Both organic and inorganic pockets (sometimes referred to as baskets or pores) could be used to store reactive and biocidal materials used for decontamination. Ultimately, taggants will be attached that are optically sensitive so that the immediate and remotely transmissible detection and differentiation of toxic materials (biological or chemical), encapsulated toxic materials, or destroyed toxins is possible.

4.2.4. Personal Physical Protection

The emerging technical advances in nanotechnology may offer opportunities to provide physical protection and enhance performance of deployed soldiers, first responders, and civilians. Current research is aimed at advanced materials and coatings that will provide protection from both ballistic threats and chemical and biological threats. The goal is a standard material capable of automatically responding to threat changes without increasing decision-making or logistical

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[165] R. Richards, et al. 2000. Consolidation of Metal Oxide Nanocrystals: Reactive Pellets with Controllable Pore Structure That Represent a New Family of Porous, Inorganic Materials. In: Journal of the American Chemical Society, Vol. 122, pp. 4921-4925.

[166] The doping (or docking) of transition metal ions of visible light chromophores (e.g., vanadium, chromium, manganese, iron, or cobalt) into the backbone of nanostructured silica (SiO_2), titania (TiO_2), silica-titania, as well as POMs has been demonstrated. Other possibilities, such as halogens, metal nanoparticles, or other POMs with particular tuned potentials could be stored in pores as special chromophores.

burdens. The solutions developed for such materials should also be applicable to other equipment such as tents and vehicles.

Leading the current effort in advancing nanoscience application to soldier safety within the US is the US Army Natick Soldier Research, Development and Engineering Center with programs including the Institute for Soldier Nanotechnologies (ISN). This program and a number of emerging efforts from other government laboratories, universities, and industry are investigating the application of nanotechnologies to develop new materials in response to battlefield threats and to monitor and respond to soldiers' health. The combined effort of all of these current research programs, and those yet to come, will be needed to deliver protective system against biological agents.

Potential capabilities for protection include the capability to block incoming threats while managing body moisture and heat to maintain comfort. New materials could accomplish these tasks on the nanoscale by using electric and magnetic fields, as well as other mechanisms, to adjust the hydrophobicity and hydrophilicity of surfaces.[167] Material surfaces may also induce nanoparticle agglomeration and clustering to promote threat sequestration and neutralization.[168]

Self-cleaning materials are an additional area of basic nanoscience research currently under exploration for direct use in protection, as well as other non-traditional applications such as commercial building materials. One approach has been to design synthetic mimics of micro- and nanotextured surfaces of hydrophobic plant leaves. Another biomimetic approach to replicate hydrophobic surfaces characterized by a combination of surface coating and roughness determines the level of water repellence and thus the self-cleaning capacity of the material. Future capabilities are suggested by the ability to tailor self-assembling surface materials with specific responses, such as de-wetting.

4.2.5. Medical Countermeasures

Operational and timely medical countermeasures are primarily intended to prevent casualties among those exposed to a biological agent. Medical countermeasures refer to therapies that can provide medical protection from a biological agent for individuals and to therapies used as part of medical management

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[167] J. Deval, et al. 2003. Reconfigurable Hydrophobic/Hydrophilic Surfaces Based on Self-Assembled Monolayers. In: Proceedings of the Materials Research Society, Vol. 774, pp. 203-208.

[168] Multifunctional nanofiber structures incorporating high-capacity selective adsorbents, such as metal organic frameworks (MOF) or metal organic polyhedras (MOP), are a route to enabling capabilities to neutralize or safely sequester hazardous breakdown products in nanoscale traps.

of casualties to enhance survivability, decrease convalescence time, and expedite return to health. Countermeasures may be deployed for field diagnosis and treatments as well. Medical systems include all pharmaceuticals, biologics, and devices for these purposes.

Among the nanotechnologies that may be exploited for medical countermeasure development are carbon nanotubes, liposomes, gene transfections, quantum dots, TiO_2, and a variety of other activated nanoparticles.[169] These materials have a multifunctional and multitasking potential that can be developed to offer better medical protection for individuals against advanced biological agents.

One example is the ability of a platform nanotechnology to swiftly deliver payloads such as gene medicines or small molecules specifically and efficiently to the target cells, which will result in a high, effective local concentration of the therapeutic agent and an immediate impact on the deleterious events. For example, targeting specificity and uptake efficiency has been demonstrated repeatedly with surface-modified nano-encapsulated materials and nanoparticles. This allows such nanomaterials to act as effective delivery vehicles for use in rapid response medical countermeasures. Moreover, the encapsulation of therapeutics within nanocomplexes serves to increase their stability in circulation, also enhancing efficacy.

This modular nanotechnology can also be engineered to be multifunctional. Multiple therapeutic agents can be pooled and encapsulated as one payload, and multiple targeting ligands can be combined on the complex. Such strategies, targeting both the specific cell population and the detrimental intracellular process, would be effective against a wide variety of biological weapons such as viral and bacterial pathogens.

Other nanotechnology capabilities identified for medical countermeasures revolve around developing suitable nanoparticles, or more generally, nanomaterials that express tailored multifunctionality, either for drug delivery or toxin adsorption. Nanoadjuvants that increase countermeasure efficacy, both pre- and post-exposure, are another route to new medical countermeasures through nanobiotechnology.

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[169] National Research Council. 2003. Giving Full Measure to Countermeasures: Addressing Problems in the DoD Program to Develop Medical Countermeasures Against Biological Warfare Agents. National Academies Press: Washington, D.C.

Recommendations

- Recognize and harvest the many benefits that are being gained, and will continue to be gained, from advances in bio- and nanotechnology.
- Support and reinforce efforts to continuously monitor science and technology developments in bio- and nanotechnology in order to identify both potential beneficial and malicious applications.

Excursus: Amateur Biology

During both project workshops, experts debated the emergence of amateur biologists communities and a “hacker culture” building up around the edges of modern biology, as well as related safety and security concerns.

The phenomenon of amateur biologists is often referenced in articles and lectures about the safety and security implications of synthetic biology, even though the vast majority of amateurs in biotechnology do not currently apply any synthetic biology techniques. Many observers associate the movement with the emerging technology field because of a shared spirit or mindset, i.e., the belief in the potential of making biology more accessible and available to a wider audience by applying engineering approaches to biology. In addition, both developments obviously center on the manipulation of DNA. There is also an affinity between amateur biologists and the International Genetically Engineered Machine competition (iGEM)[170] in particular, in which international undergraduate student teams compete in engineering biological systems. If synthetic biology succeeds in realizing its aims, the actual overlap between the two trends will certainly increase.

Characterization of the Community

The heterogeneous and growing amateur community is made up of individuals with various objectives and self-images, some of whom have considerable formal training in biology, and are interested in conducting their own research outside the confines of the traditional scientific establishment. The majority of community peers, however, are non-experts with little or no formal education in biology who do not intend to conduct research, but just want to tinker and play with biotechnology and develop simple tools, techniques, and toys.

The community is interested in building things cheaply, reducing costs, sharing information and tools, and finding ways for hobbyists to do experiments. The scope of amateur activities ranges from exploratory biology (e.g., biology kits) to constructive biology (e.g., genetic engineering) and includes tinkering with biotechnology-related hard- and software as well as so-called “wetware”, i.e., microorganisms. Examples of projects include a volunteer system for microbial biosurveillance,[171] the culturing of bioluminescent microbes,[172] the construction

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[170] www.igem.org/.

[171] www. bioweathermap.org/.

[172] http://letters.cunningprojects.com/?p=108.

of simple microbial fuel cells,[173] genotyping, etc.

The individual capabilities within the community vary greatly and it comprises scientists or expert “biohackers”, amateurs and hobbyists, inventors, entrepreneurs, artists/designers, educators, etc. According to a rough estimate by one of the proponents of the community, only a fraction of the 2,000+ amateur biologists worldwide belong to the first group of “professionals” and are graduate- or PhD-level experts who perform non-institutionalized research. These are the community members with the expertise to make enabling innovations for the other amateurs.

A bigger group of community members has undergraduate experience and is able to perform tasks such as DNA isolation/purification, polymerase chain reaction or PCR (a method for replicating DNA), tissue culturing, mutagenesis (changing the genetic information of an organism), transformation (the genetic alteration of a cell), the assembly of genetic parts, etc. The remaining, biggest part of the community uses ready-made biological kits[174] as well as procedural step-by-step guides.[175] Their first priority is not necessarily to conduct scientific research, but rather to gain hands-on experience with basic molecular and synthetic biology techniques. These activities and experiences are more like educational exercises and are often based on canonical experiments that are well understood and time-worn.

There do not seem to be any coherent efforts at present to purify and distribute critical enzymes, dyes, and other reagents these techniques depend on. Conventional supply companies, charitable scientists, and secondary markets are currently used to procure these supplies. In the future, existing or new supply companies will perhaps explicitly start serving the growing amateur market.

Community members are also interested in finding cheaper alternatives to specialist laboratory equipment, which tends to be too expensive, such as open-source PCR thermocyclers,[176] webcam-based 2-axis microscopes,[177] neuron recorders,[178] gel electrophoresis rigs, etc., and in setting up community laboratory

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[173] http://keegotech.com/products.html#MudWatt.

[174] Cf., e.g., “DNA Explorer Kit”, http://www.amazon.com/Discovery-Exclusive-DNA-Explorer-Kit/dp/B0006J31ME.

[175] Cf., e.g., “Isolation and Culture of Bioluminescent Bacteria”, http://letters.cunningprojects.com/wpcore/wp-content/uploads/2010/03/Bioluminescent%2520Bacteria%2520Culture.pdf.

[176] http://openpcr.org/; www.lava-amp.com/.

[177] http://hackteria.org/?p=52#more-52.

[178] www.backyardbrains.com/Spikerbox.aspx.

spaces to facilitate amateur involvement.[179] In 2009/2010, public labs and open hardware projects[180] collectively raised more than $53,000 from crowd-sourced funding platforms, and none of it was traditional grant money.

Several of these and other projects led to the formation of startup companies, and there are certainly precedents in other fields of “garage” activities bearing fruit and becoming the basis of multi-million dollar enterprises. There also seems to be evidence that these communities are conducting complicated and novel research, including: making weedkiller-resistant plants; cloning trees; engineering microbes that are capable of performing simple logic operations; finding novel ways to treat cancer, etc. Surprisingly little output from these efforts appears to be recorded in traditional scientific publications. Given the dispersed nature of community members, activities, and projects conducted under the “amateur” label and the lack of overview, experts identified a clear need for a more systematic and substantial review of the field and its constituents.

Community-building is mainly taking place online on a handful of different hubs.[181] In early 2010, a first conference was organized introducing some of the activities and members of the community, and trying to get a grasp and inform the public on what is actually happening in bio home labs.[182] There is a certain concentration of amateur activities in the US, but the movement is also growing in Europe and Asia and becoming more and more international with the emergence of like-minded groups of people worldwide. The US concentration can partly be explained by legal conditions, as certain kinds of activities, for instance such that involve genetic engineering or certain organisms (e.g., E. coli), are forbidden in other parts of the world, including Western Europe.

The community takes inspiration from and emphasizes the analogy with other examples of constructive uses of technology by individuals, in particular with developments in computer and information technology. Beyond the increasing importance of information technology for modern biotechnology, there are several similarities between the two technology trends, including the emergence of an individualistic subculture of computer- or bio-hackers, respectively.

It has been argued that progress in traditional biology has been impeded

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[179] www.biocurious.org/index.php?title=About_BioCurious.

[180] I.e., Biocurious, OpenPCR, and the LavaAmp; cf. www.biocurious.org/; http://openpcr.org/; www.lava-amp.com/.

[181] E.g., diybio.org; biopunk.org; hackteria.org; biocurious.org. See also http://groups.google.com/group/diybio/ and www.openwetware.org/wiki/DIYbio.

[182] Outlaw biology? Public Participation in the Age of Big Bio, Los Angeles, January 2010. http://outlawbiology.net/

because it has not been supported by an amateur counterpart and that a vibrant amateur sector could help reinforce advances in biotechnology. Do-it-yourself biology gives individuals a hands-on relationship with biotechnology and decreases the suspicion towards “big science”. It is one of the stated goals of the amateur community to increase the human capital in biotechnology and improve the interface between science and society.

Safety and Security Concerns

Concerns about the amateur movement or “bio-hackers” mainly center on two scenarios: either an accidental or an intentional release of bioengineered organisms. On the one hand, ill-considered or dangerous experimentation by a reckless or inexperienced individual without malicious intentions could have hazardous consequences for the environment or the neighboring community. On the other hand, a malevolent amateur with a grudge against individuals, groups, or society as whole may want to demonstrate his technical skills and prove something to the world by intentionally releasing disease-causing organisms.[183]

Workshop participants felt that, given the current state and capabilities of the amateur community, both scenarios seem to be exaggerated and the potential for harm rather low at the moment. It was noted that the negative framing of the movement by the press is distorting the actual capabilities and risks of do-it-yourself biology and is “incorrectly” mixing it with synthetic biology, as noted above.

There is certainly no need to raise the alarm; nevertheless, thinking about and addressing potential problems early enough seems to be prudent. If biotechnology becomes more accessible under the guise of synthetic biology, things that are currently beyond the technical capabilities of someone working outside the laboratory environment will likely become feasible in the future and make the issue more pressing. According to experts, a certain and likely growing level of risk in the medium to long term stemming from activities commonly labeled amateur or garage biology cannot be denied and should be calmly addressed now.

Participating experts quoted biosafety issues and public perception as the main near-term areas of concern with regard to the movement and its activities. Being aware of and following basic biosafety standards and related national regulations, such as the proper disposal of waste, is something the community and its members should ensure. A simple biosafety event, be it an accident or an irresponsible act, even without any potential for doing harm, could ignite public

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[183] See also J.B. Tucker and R.A. Zilinskas. 2006. The Promise and Perils of Synthetic Biology. In: The New Atlantis, Spring 2006, pp. 25-45.

uproar and put pressure on policy-makers to react. This could lead to a ban on certain activities and hamper the further development of the movement. It could also cause collateral damage to science and industry by negatively affecting the public attitude towards synthetic biology and related fields as a whole. The possibility that do-it-yourself biology may cause chilling effects for the gene synthesis industry, similar to the experiences made with genetically modified organisms in Europe, is in fact a concern of commercial DNA suppliers.

The issue of “bio-hackers” is commonly associated with amateur or do-it-yourself biology. The term has been often used in association with those who would use biology maliciously or irresponsibly. However, the term is misleading; and among many, especially younger people the term is not negatively connoted, but used to describe those who think and act “outside the box” and pursue biology outside the bounds of the traditional scientific framework.

Addressing the Concerns

Experts noted that it is important not to scare people and policy-makers, which could easily happen when talking about garage biology and the availability of DNA by order from commercial dealers in the same breath, and to adopt an affirmative but critical and careful language when talking about these issues. It was noted that the community could certainly do better than in the past, and the experts called for the concerns of society to be taken more seriously and addressed upfront, even if they are considered to be baseless. In its own best interest and in order to avoid public backlash, the community should clearly show that it engages in safety and security issues and takes them seriously. It was acknowledged that the community has to strive for a careful balance in showing responsibility and engaging in public dialogue while keeping its independence and alternative self-perception.

Experts agreed that the main focus in dealing with the concerns associated with the amateur biologists movement must be prevention. Most important in this regard are outreach and education activities with the aim of raising the awareness of community members for safety and security issues and convincing them that there is something at stake and a purpose to be served by engaging and dealing with some of the potential risks. Assisted and empowered in such a way, the community could, on its own or in partnership with other actors, draft its own standards and “governance” models without losing its independence and alternative mindset.

Among other things, such measures could include transparency and safety norms, a community code of conduct, biosafety practices that are easy to adhere to, or a community point of contact for members where safety advices could be offered if needed and red flags be raised in case dangerous or suspicious activities are noted. The latter could also act as a junction between the community and external actors. Experts underlined the importance that the science and security communities act and be seen as a resource for the community and not primarily as watchdogs.

In addition to these points, which center on community engagement and self-imposed actions, experts noted that at some point in the future, it might be necessary to think about specific kinds of regulations, licensing mechanisms, etc. for certain activities. However, while this possibility certainly cannot be entirely neglected, it should be approached reasonably and thoughtfully, as it bears the risk of driving certain activities underground and tearing the movement apart. Of course, existing laws and regulations apply, and awareness of them within the community is important.

Experts felt that any attempt to address the issues of concern regarding amateur biologists should be based on the involvement of the community in one form or another. Community-building as it is currently happening should be welcomed and will be an important part of any "solution" to some of the concerns, rather than part of the problem, as implied by some observers. Whether through outreach and education activities or the drafting of some sorts of regulations, etc., securing the understanding and support of the community is crucial and makes the implementation of measures more likely to succeed. The phenomenon of amateur biology is real and happening anyway. Experts felt that it is better to shape the development of the community and have a communication channel than to alienate it and make it go underground.

Community members themselves have started taking steps to address some of the concerns raised and to reinforce a responsible culture within the movement as well as to promote what they call good "bio-citizenship". They have committed themselves to establish transparency and safety norms, draft a community code of conduct or manifesto as well as guidelines on biosafety and legal issues, and organize "positive community projects", e.g., the nomination of poster projects or biosafety "champions".

As a first step in that direction, the founders of "diybio.org" – one of the community hubs – are currently implementing a one-year project in collaboration with the Alfred P. Sloan Foundation and the "Synthetic Biology Project" of the Woodrow Wilson Center with the goal of developing a long-term roadmap towards a positive culture of safety and security within do-it-yourself biology worldwide.[184] In particular, the project aims at defining the community and its activities; inventorying existing ethical codes of conduct; identifying potential

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[184] See also J.B. Tucker and R.A. Zilinskas. 2006. The Promise and Perils of Synthetic Biology. In: The New Atlantis, Spring 2006, pp. 25-45.

risks posed by amateur biology; developing preliminary biosafety guidance; and mobilizing and celebrating good biosafety practices within the community.

There are also plans to establish a safety and security working group within the community, and it already receives informal advisory support from some renowned scientists to give it greater academic grounding. Bridges and collaborations are also being built between the diybio.org project and US regulatory and enforcement agencies, such as the FBI. In addition, community repre-sentatives have taken part in the two workshops organized in the framework of this UNICRI/EC risk and response assessment project, which shows their willingness to engage and commit themselves in a security dialogue. All of these activities by the amateur community were well noted and welcomed during both workshops.

Recommendations

- Support community-building and engage with the amateur biology community on a continuous basis to understand their motivation, activities, and needs better as well as to create an environment in which their activities are pursued safely and securely.
- In partnership with the community, design and implement tailored outreach and education activities to raise the awareness of community members on safety and security issues, as well as relevant international and national rules and regulations.
- Encourage and actively support the development of community-based standards, good practices, codes of conduct, and information material for community members, mainly - but not exclusively - relating to biosafety, transparency, and legal norms.
- Foster the establishment of a community point of contact or communication channel for both community members and external stakeholders, and improve the sharing of information between relevant communities, including authorities.

Conclusions

In the course of this project, experts identified a number of potential avenues for technology misuse, at varying degrees of likelihood and difficulty, that are either enabled or facilitated by technological advances in synthetic biology and nanobiotechnology. Some of these advances pave the way for entirely new possibilities, while others provide alternative (and perhaps easier) development pathways for goals that are already achievable using alternative technology options.

In the short term, it is highly unlikely that non-state actors would choose one of these high technology pathways over easier means of acquiring and employing bioweapons or alternative (conventional) attack options. While the likelihood might increase in specific cases in the medium term, as the technologies mature, the potential and capabilities for misuse are likely negligible, and a myriad of beneficial applications can be expected to emerge.

While most of the tools and techniques necessary to facilitate the acquisition of bioweapons are not within reach of small groups in the short to medium term, some of them are certainly within the capabilities of large organizations or states, should they choose to go down that path. In the longer term, if the potential of synthetic biology (and of nanobiotechnology, to a certain extent) to make biotechnology more reliable, easier, cheaper, and faster is realized, there could be a significant risk of hostile applications by both state and non-state actors.

By reducing the time and resources needed to go from concept to application, advances in synthetic biology and nanobiotechnology might significantly lower the barriers to the acquisition of an offensive bioweapons capability and reduce the likelihood of such activities being uncovered. In synthetic biology and nanobiotechnology, as in biotechnology in general, the same resources and knowledge applied for the betterment of humanity can be misused to deliberately cause harm. Almost every potential security risk discussed during this project results from completely legitimate research endeavors and developments, even with regard to issues such as pathogenicity or the suppression/overstimulation of the immune system. The adaptation of legitimate work for hostile purposes was said to be fairly straightforward in most areas, and the differentiation of peaceful from hostile applications of biotechnology will likely be further complicated by the dawn of synthetic biology and nanobiotechnology.

Synthetic biology and nanobiotechnology might have a considerable impact on bioweapons proliferation. To a certain extent, the nature of progress in biotechnology will, if it has not already done so, negate the ability to control the technology with traditional means. Expertise, materials, and equipment are already available in varying degrees around the globe and, accordingly, the proliferation of knowledge and expertise – although not necessarily weapons-related – has already taken place. If synthetic biology realizes its aims of making biotechnology more accessible, it is very likely that relevant knowledge, equipment, and personnel will further spread to new geographical locations and societal sectors.

In addition, the technical possibilities enabled or facilitated by synthetic biology and nanobiotechnology might increase the perceived utility and hence the appeal of bioweapons by improving their reliability and controllability. The nature of advances in bio- and nanotechnology as well as the consequences of the ability to engineer bioweapons as desired could challenge current arms control norms and instruments, in particular the Biological Weapons Convention (BWC).

This assessment of long-term developments is based not so much on the implications of the individual technology risks examined, as neither seems to add an entirely new dimension to the spectrum of biological (weapons) threats for the foreseeable future; instead, synthetic biology can be seen as an "enabling technology" that will likely simplify the practice of, and reduce the entry hurdles to, biotechnology, making it more accessible and widespread. It might enable more actors with malicious intent to pursue bioweapons, allowing them to modify biological systems with greater ease, reliability, speed, and at lower costs.

It is with regard to this "enabling/proliferation aspect" and the resulting broad societal diffusion of biotechnological capabilities, including the emergence of a subculture outside traditional confines, that synthetic biology might have to be considered a "game-changer" in the long term, with both positive and negative implications. In this sense, synthetic biology and nanobiotechnology may constitute the initial steps towards a qualitative and quantitative paradigm shift in biotechnology and could revolutionize the manner in, and scale at, which biology will be applied in the future.

To tackle the potential negative long-term implications of progress in biotechnology, the international community should strengthen the established norms and taboos against bioweapons development and use. In addition, the majority of experts that participated in this assessment suggested that the international community should also begin to move beyond efforts to regulate and control these developments towards managing them more comprehensively by complementing traditional approaches with innovative initiatives and concepts.

The focus should be shifted towards creating a shared responsibility of politics, industry, science, and society to reinforce a culture of safety and security in biotechnology. The risks should be minimized by engaging relevant communities and empowering them to detect and report abuses. This requires fostering a worldwide culture of awareness and responsibility in biotechnology as well as building a network of relevant public and private actors, top-down and bottom-up measures, initiatives, and checks on the national and international levels covering all relevant activities and linking all levels of society in a comprehensive and systematic way.

Such an approach would be unprecedented in the history of technology and arms control and requires a common, yet flexible strategy to act in concert. It might be facilitated by the establishment of an international authority that, instead of providing legally binding arms control mechanisms and compliance assurances, works with states and stakeholders on issues such as outreach, education, and awareness-raising; science and technology monitoring; good practices in biosafety and biosecurity; laws and regulations; international harmonization and universalization of measures, etc.; and that coordinates and promotes the international portfolio of respective efforts.

Finally, it is important that efforts to tackle the potential negative implications of advances in biotechnology do not impede beneficial research. The net effect of developments in biotechnology could certainly prove to be advantageous – also in terms of countering the bioweapons threat – and beneficial applications thus should be considered an important variable in the overall risk assessment.

Annexes

Experts

Experts who participated in the project and contributed to this report:

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Glossary[185]

Aerosol[186]

1. A suspension of fine solid or liquid particles in gas. 2. A substance dispensed from a pressurized container as an aerosol.

Adjuvant[187]

A substance added to a vaccine to improve the immune response so that less vaccine is needed to provide protection.

Amyloid[188]

A waxy translucent substance consisting of a protein in combination with polysaccharides that is deposited in some organs and tissue under abnormal conditions (as in Alzheimer's disease).

Anion[189]

The ion in an electrolyzed solution that migrates to the anode; broadly, a negatively charged ion.

Anthrax[190]

Anthrax is a zoonotic disease caused by Bacillus anthracis. Humans may be infected by consuming infected meat (gastrointestinal anthrax), by skin contact with contaminated animal wool, skin or tissue (cutaneous anthrax) or by the inhalation of infected spores deep into the lungs (pulmonary or inhalation anthrax). Anthrax has traditionally been a preferred agent for biological weapons development owing to its ease of acquisition and cultivation as well as its lethality and hardy nature.

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[185] Unless otherwise stated, the following definitions are taken from the Food and Agriculture Organization (FAO) Glossary of Biotechnology for Food and Agriculture, www.fao.org/biotech/index_glossary.asp; the World Health Organization (WHO) Register of Health Topics, www.who.int/topics/en/; the WHO Glossary of globalization, trade and health terms, www.who.int/trade/glossary/en/; or from the United Nations Interregional Crime and Justice Research Institute (UNICRI).

[186] US National Institutes of Health (NIH), US National Library of Medicine, MedlinePlus Medical Dictionary, www.nlm.nih.gov/medlineplus/mplusdictionary.html (NIH MedlinePlus).

[187] US Department of Health and Human Services, Flu Glossary, http://www.flu.gov/glossary/.

[188] US National Institutes of Health (NIH), US National Library of Medicine, Genetics Home Reference Glossary, http://ghr.nlm.nih.gov/glossary (NIH GHR).

[189] Ibid.

[190] Foreign Affairs and International Trade Canada, Global Partnership Program, Glossary of Terms, http://www.international.gc.ca/gpp-ppm/glossary-glossaire.aspx.

Antibiotic
A class of natural and synthetic compounds that inhibit the growth of, or kill some microorganisms. Antibiotics are widely used medicinally to control bacterial pathogens, but resistance in bacteria to particular antibiotics is often rapidly acquired through mutation.

Antigen
A macromolecule (usually a protein foreign to the organism), which elicits an immune response on first exposure to the immune system by stimulating the production of antibodies specific to its various antigenic determinants. During subsequent exposures, the antigen is bound and inactivated by these antibodies.

Anti-microbial resistance
Resistance occurs when microbes develop methods to survive the use of medicines meant to kill or weaken them. The development of anti-microbial resistance is a natural biological phenomenon, however, humans can and do increase the likelihood of it happening.

Artemisinin
Chemical compound extracted from the leaves of the plant Artemisia annua (sweet wormwood), also known as qinghaosu, used in antimalarial medicines.

Assay
1. To test or evaluate. 2. The procedure for measuring the quantity of a given substance in a sample (chemically or by other means).

A:T – C:G[191]
Adenine (A) and thymine (T) are two of the four chemical bases in DNA, the others being cytosine (C), and guanine (G). DNA bases pair up with each other, A with T (A:T) and C with G (C:G), to form units called base pairs.

Bacterium (pl.: bacteria)
Unicellular prokaryotic organisms, without a distinct nucleus. Major distinctive groups are defined by Gram staining. Also classified on the basis of oxygen requirement (aerobic vs. anaerobic) and shape.

Bacteriophage (also: phage)
A virus that infects bacteria. Altered forms are used as cloning vectors.

Base pair (abbreviation: bp)
The two separate strands of a nucleic acid double helix are held together by

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[191] NIH GHR.

specific hydrogen bonding between a purine and a pyrimidine, one from each strand. The base A pairs with T in DNA (with U in RNA); while G pairs with C in both DNA and RNA. The length of a nucleic acid molecule is often given in terms of the number of base pairs it contains.

Bio-engineering
See ‘Biotechnology’.

Biological agents and toxins
Biological agents and toxins are (naturally occurring or engineered) disease-causing organisms or toxins which kill or harm humans, animals or plants. Includes genetic elements or subunits thereof regardless of origin or method of production. The definition includes bacteria, viruses, fungi, prions and rickettsiae.

Biological weapons
Biological weapons are devices, which disseminate disease-causing organisms or toxins to kill or harm humans, animals or plants. Generally comprises two parts – an agent and a delivery device.

Bioluminescence
The enzyme-catalyzed production of light by a number of diverse organisms (e.g. fireflies and many deep ocean marine organisms). Utilized as a reporter gene in plant transgenesis, and for the detection of food-borne pathogenic bacteria.

Biomolecular nanotechnology[192]
Nanotechnology existing in living systems and resulting from our ability to use biomolecules as components for molecular nanotechnology.

Biotechnology
1. Any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use.
2. In a narrow sense, a range of different molecular technologies such as gene manipulation and gene transfer, DNA typing and cloning of plants and animals.

Boron[193]
A trivalent metalloid element found in nature only in combination and used in metallurgy and in composite structural materials.

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[192] Nanoword, Encyclopedia Nanotech, www.nanoword.net/pages/encyclopedia.php.

[193] NIH MedlinePlus.

Botulinum
Clostridium botulinum is a gram positive, obligate anaerobic, spore-forming, rod-shaped bacterium, commonly found in soils and marine sediments throughout the world. It also colonizes the gastro-intestinal tract of fishes, birds and mammals. Botulinum is used as pharmaceutical for human use (agent acting on the nervous system) or as a biological warfare agent. It causes botulism, a disease characterized by symmetrical, descending, flaccid paralysis of motor and autonomic nerves usually beginning with cranial nerves.

Bovine spongiform encephalopathy
Bovine spongiform encephalopathy (BSE) is a transmissible, neurodegenerative, fatal brain disease of cattle. The disease has an incubation period of 4-5 years, but death usually occurs within months of disease onset. BSE has been linked to the appearance in humans of variant Creutzfeldt-Jakob disease.

Capsid
The protein coat of a virus. The capsid often determines the shape of the virus.
Carbon nanotube
A nanotube consisting of carbon (see also ‘Nanotube’).

Cassette
An engineered chimeric DNA designed to be transferred into a cell or tissue. Typically, the cassette comprises the gene or genes of interest, a marker gene and appropriate control sequences as a single package.

Catalyst
A substance that promotes a chemical reaction by lowering the activation energy of a chemical reaction, without itself undergoing any permanent chemical change.

Chimeric DNA
A recombinant DNA molecule that contains sequences from different organisms.

Cell line
1. A cell lineage that can be maintained in vitro. Significant genetic changes can occur during lengthy periods in culture, so that the genotype of long-term cell lines may not be the same as that of the starter cell. 2. A cell lineage that can be recognized in vivo.

Chemical weapons
Chemical weapons are devices, which can cause death or other harm through the toxic properties of toxic chemicals or their precursors that the device releases.

Chromosome
In eukaryotic cells, chromosomes are the nuclear bodies containing most of the genes largely responsible for the differentiation and activity of the cell. Chromosomes contain most of the cell's DNA in the form of chromatin. Each eukaryotic species has a characteristic number of chromosomes. Bacterial and viral cells contain only one chromosome, which consists of a single or double strand of DNA or, in some viruses, RNA, without histones.

Coat protein
See 'Capsid'.

Codon
One of the groups of three consecutive nucleotides in DNA or messenger RNA, which represent the unit of genetic coding by specifying a particular amino acid during the synthesis of polypeptides in a cell.

Cytosol
The fluid portion of the cytoplasm, i.e. the cytoplasm minus its organelles.

DNA
Abbreviation for deoxyribonucleic acid. DNA constitutes the genetic material of most known organisms and organelles, and usually is in the form of a double helix, although some viral genomes consist of a single strand of DNA, and others of a single- or a double-stranded RNA.

DNA replication
The process whereby DNA copies itself, under the action of and control of DNA polymerase.

DNA sequence/sequencing
The linear order of nucleotides along a DNA or RNA molecule, and the process of obtaining this. Genome sequencing aims to generate the linear order of all nucleotides present in the nuclear DNA of an organism.

DNA shuffling[194]
DNA shuffling is a method for in vitro recombination of homologous genes. The genes to be recombined are randomly fragmented, purified and reassembled.

DNA synthesis (de novo)
The creation of new DNA strands from chemical components and not through DNA replication.

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[194] Adapted from Joern J. M. 2003. DNA Shuffling. In: F. Arnold and G. Georgiou (eds.). 2003. Directed Evolution Library Creation, Methods in Molecular Biology, Vol. 231, I, pp. 85-89.

DNA synthesizer
A machine that chemically synthesizes DNA sequences.

DNAzymes (also: DNA enzymes)[195]
DNAzymes are DNA-based biocatalysts capable of performing chemical transformations. These catalysts have not been found in nature, and all known DNAzymes were isolated by in vitro selection. Most of their substrates are nucleic acids and can therefore provide additional control over nucleic-acid-based nanodevices.

Double-stranded DNA (abbreviation: dsDNA)
Two complementary strands of DNA annealed in the form of a double helix.

Drug resistance
See 'Anti-microbial resistance'.

Dual-use biotechnologies
Dual-use biotechnologies are facilities, equipment, materials and other technology directly associated with biological materials, which have potential for both beneficial and detrimental applications.

Ebola[196]
Any of several single-stranded RNA viruses of the family Filoviridae (filovirus) of African origin that cause an often fatal hemorrhagic fever.

Edema factor[197]
The portion of the anthrax toxin, which produces edema when combined with protective antigen.

Electrophoresis
A ubiquitous molecular biology technique, with many variants, used to resolve complex mixtures of macromolecules into their components. Its principle is to subject samples to an electric field applied across a porous matrix. Molecules will migrate under these conditions at a rate dependent on their net electric charge and/or their molecular weight.

Enzyme
A protein that catalyzes specific chemical reactions but is not used up in the

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195 Adapted from Yi Lu and Juewen Liu. 2006. Functional DNA nanotechnology: emerging applications of DNAzymes and aptamers. In: Current Opinion in Biotechnology, 17, pp. 580-588.

196 NIH MedlinePlus.

197 www.csa.com/discoveryguides/anthrax/gloss.php.

reaction. Enzymes are classified into six major groups, according to the type of reaction they catalyze: oxidoreductases; transferases; hydrolases; lyases; isomerases; ligases.

Escherichia Coli (abbreviation: E. Coli)
A commensal bacterium inhabiting the colon of many animal species, including humans. E. Coli is widely used as a model of cell biochemical function, and as a host for cloning DNA. Some strains are significant pathogens.

False negative
A negative assay result that should have been positive.

False positive
A positive assay result that should have been negative.

Fullerene[198]
A Fullerene is a pure carbon molecule composed of at least 60 atoms of carbon. They are cage-like structures of carbon atoms.

Gene
The unit of heredity transmitted from generation to generation during sexual or asexual reproduction. More generally, the term is used in relation to the transmission and inheritance of particular identifiable traits. The simplest gene consists a segment of nucleic acid that encodes an individual protein or RNA.

Genome
1. The entire complement of genetic material (genes plus non-coding sequences) present in each cell of an organism, virus or organelle. 2. The complete set of chromosomes (hence of genes) inherited as a unit from one parent.

Genomics
The research strategy that uses molecular characterization and cloning of whole genomes to understand the structure, function and evolution of genes and to answer fundamental biological questions.

Genotype
The genetic constitution of an organism.

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[198] Dictionary of nanotechnology, www.nanodic.com (Nanodictionary).

Hydrogen[199]
A nonmetallic element that is the simplest and lightest of the elements and that is normally a colorless odorless highly flammable diatomic gas.

Hydrophilicity
Describes a molecule or part of a molecule that dissolves readily in water.

Hydrophobicity
Describes a molecule or part of a molecule that does not dissolve in water.

Immune system[200]
The body's defense mechanism against foreign organisms or substances and deviant native cells. It includes the humoral immune response and the cell-mediated response and consists of a complex of interrelated cellular, molecular, and genetic components.

Influenza
Influenza is a viral infection that affects prevalently the nose, throat, bronchi and, occasionally, lungs. Infection usually lasts for about a week, and is characterized by sudden high fever, aching muscles, headache and severe malaise, non-productive cough, sore throat and rhinitis. The virus is easily transmitted from person to person via droplets and small particles produced when infected people cough or sneeze.

Inorganic compound
Historically, chemicals that could not be derived from living processes. In modern usage, chemicals that do not contain carbon, although carbonates and a few other simple carbon compounds are generally regarded as inorganic.

In vitro
Outside the organism, or in an artificial environment. Applied for example to cells, tissues or organs cultured in glass or plastic containers.

In vivo
The natural conditions in which organisms reside. Refers to biological processes that take place within a living organism or cell under normal conditions.

In silico
In a computer file. In the present context, the use of data bases of DNA and

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[199] NIH MedlinePlus.

[200] NIH GHR.

protein sequence to help answer biological questions. This is growing area of biology as the amount of genomics and proteomics data continues to grow.

Ion channel
A protein integral to a cell membrane, through which selective ion transport occurs.

Isolate[201]
An individual (as a spore or single organism), a viable part of an organism (as a cell), or a strain that has been isolated (as from diseased tissue, contaminated water, or the air); also, a pure culture produced from such an isolate.

Lab-on-a-chip[202]
A lab-on-a-chip is a device that integrates one or several laboratory functions on a single chip of only millimeters to a few square centimeters in size for handling extremely small fluid volumes.

Lethal factor[203]
Virulence factor of the anthrax toxin that, when combined with protective antigen, results in death of the host.

Ligand
A small molecule (e.g. activators, substrates and inhibitors of enzyme activity) bound to a protein by non-covalent forces; an ion or a molecule that binds to another chemical entity to form a larger complex.

Liposome
A synthetic microscopic spherical structure consisting of a phospholipid bilayer membrane containing a user-defined aqueous solution. Liposomes can be used to transport relatively toxic drugs into diseased cells, where they can exert their maximum effect. DNA molecules may be entrapped in, or bound to the surface of, the vesicles, and subsequent fusion of the liposome with the cell membrane will deliver the DNA into the cell. Liposomes have been used to develop an efficient transfection procedure.

Locus
A site on a chromosome.

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[201] NIH MedlinePlus.

[202] Nanodictionary.

[203] www.csa.com/discoveryguides/anthrax/gloss.php.

Metabolic pathway[204]

Any series of connected reactions occurring in a cell or organism. Its reactants, intermediates, and products are called metabolites. There are over 2000 known metabolic reactions, each catalyzed by a distinct enzyme. The types of enzymes and metabolites vary with the identity of the organism, the cell type, its nutritional status, and its developmental stage. Many metabolic pathways are branched and interconnected, and finding a metabolic pathway out of thousands of reactions has been one of the main research agendas of biochemistry.

Methamphetamine (also: meth; speed)

Methamphetamine is an amphetamine-type stimulant (ATS) belonging to a group of drugs, such as methcathinone, fenetylline, ephedrine, pseudoephedrine, methylphenidate and MDMA or 'Ecstasy' – an amphetamine-type derivative with hallucinogenic properties. The use of ATS is a global and growing phenomenon and in recent years, there has been a pronounced increase in the production and use of ATS worldwide. Over the past decade, abuse of ATS has infiltrated its way into the mainstream culture in certain countries.

Microbe

See 'Microorganism'.

Micro-electromechanical system (MEMS)[205]

Refers to machines with moving parts smaller than a human hair that contain both electrical and mechanical components on silicon. MEMS are used to integrate various electro-mechanical functions onto integrated circuits. A typical MEMS device combines a sensor and a control logic to perform a monitoring function. Examples include sensing devices used to control the deployment of airbags in cars and switching devices used in optical telecommunications cables.

Microorganism

Organism visible only under magnification (e.g. bacteria, parasites, fungi, viruses, etc.).

Mousepox virus (also: Ectromelia virus)[206]

A highly contagious disease of mice that is caused by a poxvirus of the genus orthopoxvirus.

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204 National Institutes of Health (NIH), Stadtman Glossary, http://history.nih.gov/exhibits/stadtman/glossary.htm.

205 Nanodictionary.

206 NIH MedlinePlus.

Mutagenesis
Induction of heritable change(s) in the genetic constitution of a cell through alterations to its DNA.

Mycoplasma mycoides
Mycoplasma mycoides JCVI-syn 1.0 is the world's first synthetic bacteria, created by the J. Craig Venter Institute (JCVI) in May 2010.

Nanoadjuvant
See 'Adjuvant'.

Nanobiotechnology[207]
Nanobiotechnology is a field that applies the nanoscale principles and techniques to understand and transform biosystems (living or non-living) and which uses biological principles and materials to create new devices and systems integrated from the nanoscale.

Nanocapsules (also: nanocontainers)[208]
Nanocapsules are submicroscopic colloidal drug carrier systems composed of an oily or an aqueous core surrounded by a thin polymer membrane.

Nanocarriers[209]
Nanocarriers are colloidal particulate systems with size ranging between 10-1000nm. They have been successfully utilized in the diagnosis, treatment and monitoring of various diseases.

Nanodot
See 'Quantum dot'.

Nanomaterials[210]
Material with one or more external dimensions, or an internal structure, on the nanoscale, which could exhibit novel characteristics compared to the same material without nanoscale features.

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[207] M.C. Roco. 2003. Nanotechnology: convergence with modern biology and medicine. In: Current Opinion in Biotechnology, 14, p. 337.

[208] Couvreur P., Barratt G., Fattal E., Legrand P. and Vauthier C. 2002. Nanocapsule technology: a review. In: Crit Rev Ther Drug Carrier Syst., 19(2), pp. 99-134.

[209] Oberdorster G., Oberdorster E. and Oberdorster J. 2005. Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles. In: Environ Health Perspect, 113(7), pp. 823-839.

[210] Nanodictionary.

Nanometer (nm)[211]
A unit of length equal to one billionth of a meter or one millionth of a millimeter. It is denoted as nm.

Nanoparticles[212]
Nanoparticles are particles of less than 100nm in diameter that exhibit new or enhanced size-dependent properties compared with larger particles of the same material.

Nanoscale
The nanoscale ranges from 0.1nm to 100nm.

Nanoscience[213]
Study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at a larger scale.

Nanoshell [214]
A nanoparticle composed of a metallic shell surrounding a semiconductor. When nanoshells reach a target cancer cell, they can be irradiated with near-infrared light or excited with a magnetic field, either of which will cause the nanoshell to become hot, killing the cancer cell.

Nanotechnology[215]
Nanotechnologies are the design, characterization, production and application of structures, devices and systems by controlling shape and size at the nanometer scale.

Nanotube[216]
A nanoscale tube-like structure which can be found naturally in some minerals or be man-made from a variety of materials including carbon.

Nanowire[217]
Nanometer-scale wire made of metal atoms, silicon, or other materials that con-

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[211] Ibid.

[212] Ibid.

[213] Ibid.

[214] Ibid.

[215] Ibid.

[216] Ibid.

[217] Ibid.

duct electricity. They can be coated with molecules such as antibodies that will bind to proteins and other substances of interest to researchers and clinicians. By the very nature of their nanoscale size, nanowires are incredibly sensitive to such binding events and respond by altering the electrical current flowing through them, and thus can form the basis of ultra sensitive molecular detectors.

Nebulizer
A nebulizer turns a liquid (medicine) into fine droplets (in aerosol or mist form) that are inhaled through a mouthpiece or mask.

Nucleic Acid
A macromolecule consisting of polymerized nucleotides. Two forms are found, DNA and RNA. Nucleic acids may be linear or circularized, and single- or double-stranded.

Nucleotide
A nucleoside with one or more phosphate groups linked at the 3'- or 5'-hydroxyl of a pentose sugar. When the sugar is ribose, the nucleotide is a ribonucleotide; when it is 2-deoxyribose, the nucleotide is a deoxyribonucleotide. RNA and DNA are polymers of, respectively, ribonucleoside 5'-monophosphates and deoxyribonucleoside 5'-monophosphates. Nucleotides containing the bases adenine, guanine and cytosine (A, G, C) occur in both DNA and RNA; thymine (T) occurs only in DNA, and uracil (U) only in RNA.

Oligonucleotide
A nucleotide oligomer. Often synthesized for use as primers for in vitro DNA synthesis.

Pandemic[218]
The worldwide outbreak of a disease in humans in numbers clearly in excess of normal.

Pathogen
A disease-causing organism (generally microbial: bacteria, fungi, viruses; but can extend to other organisms: e.g. nematodes etc.).

Peptide[219]
Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins.

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[218] US Department of Health and Human Services, Flu Glossary, http://www.flu.gov/glossary/.

[219] NIH GHR.

Phage
See ‘Bacteriophage’.

Photocatalysis[220]
The acceleration of a chemical reaction by radiant energy (as light) acting either directly or by exciting a substance that in turn catalyzes the main reaction.

Photosensitization[221]
Photochemical or photophysical alteration occurring in one molecular entity as a result of initial absorption of radiation by another molecular entity called a photosensitizer.

Photosensitizer
See ‘Photosensitization’.

Plasmid
A circular self-replicating non-chromosomal DNA molecule found in many bacteria, capable of transfer between bacterial cells of the same species, and occasionally of different species. Antibiotic resistance genes are frequently located on plasmids. Plasmids are particularly important as vectors for genetic engineering.

Poliovirus
Poliovirus is a human enterovirus that causes Poliomyelitis (polio), a highly infectious viral disease.

Polymerase chain reaction (abbreviation: PCR)
A widespread molecular biology procedure that allows the production of multiple copies (amplification) of a specific DNA sequence, provided that the base pair sequence of each end of the target is known. It involves multiple cycles of DNA denaturation, primer annealing, and strand extension, and requires a thermostable DNA polymerase, deoxyribonucleotides, and specific oligonucleotides (primers).

Polymer
A macromolecule synthesized by the chemical joining of many identical or similar monomers. For example, amino acids, monosaccharides and nucleotides give rise to proteins, polysaccharides and nucleic acids respectively. Water is eliminated between the monomers as they link to form chains.

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[220] NIH MedlinePlus.

[221] S. E. Braslavsky. 2007. Glossary of terms used in photochemistry. In: Pure Appl. Chem., 79(3), pp. 293-465.

Polymorphism
The occurrence of allelic variation at a locus. Polymorphism in nucleotide sequences has provided powerful diagnostic tools.

Precursor chemical[222]
A chemical that can be chemically combined with another substance to form a chemical warfare agent or other compounds. Most precursors controlled through non-proliferation initiatives also have commercial uses.

Prion
Believed to be the agent responsible for the class of diseases called spongiform encephalopathy, including scrapie in sheep, bovine spongiform encephalopathy (BSE; mad cow disease) in cattle and Creutzfeldt-Jakob disease (CJD) in humans. It is an abnormal form of a brain protein, and has no detectable nucleic acid content.

Protective antigen[223]
A component of the anthrax toxin that combines with lethal factor and edema factor to mediate their entry into the cell.

Protein
A macromolecule composed of one or more polypeptides, each comprising a chain of amino acids linked by peptide bonds.

Protein engineering
Generating proteins with modified structures that confer novel properties such as higher catalytic specificity or thermal stability.

Quantum dot[224]
A dot with an extension of several nanometer constructed of metallic or semiconductive material describing a nearly zero-dimensional object. These quantum dots have unique electrical properties, which can be used to store electrons for example or to transform the color of light. The quantum dot is considered to have greater flexibility than other fluorescent materials, which makes it suited to use in building nanoscale computing applications where light is used to process information. They are made from a variety of different compounds, such as cadmium selenide.

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[222] Foreign Affairs and International Trade Canada, Global Partnership Program, Glossary of Terms, http://www.international.gc.ca/gpp-ppm/glossary-glossaire.aspx.

[223] www.csa.com/discoveryguides/anthrax/gloss.php.

[224] Nanodictionary.

Reactive oxygen species (ROS)[225]
Molecules or ions formed by the incomplete one-electron reduction of oxygen. These reactive oxygen intermediates include singlet oxygen; superoxides; peroxides; hydroxyl radical; and hypo-chlorous acid. They contribute to the microbicidal activity of phagocytes, regulation of signal transduction and gene expression, and the oxidative damage to nucleic acids; proteins; and lipids.

Recombinant DNA
The result of combining DNA fragments from different sources. Recombinant DNA techniques are widely used to manipulate DNA, including: the identification and cloning of genes; the study of the expression of cloned genes; and the production of large quantities of gene products.

Replication
The in vivo synthesis of double-stranded DNA by copying from a single-stranded template.

Resistance
The ability to withstand abiotic (high temperature, drought etc.) or biotic (disease) stress, or a toxic substance. Often in the context of genetic determination of resistance.

Ribosome
The sub-cellular structure that contains both RNA and protein molecules and is the site for the translation of messenger RNA into protein.

Ribosome-inactivating proteins
A class of plant proteins that inhibit normal ribosome function, and are thus highly toxic. Type 1 RIPs consist of single polypeptide chain proteins; type 2 (e.g. ricin) consist of two proteins linked by a disulphide bridge, one of which is the toxin and the other a lectin that attaches to recognition sites on a target cell.

Ricin[226]
A poisonous protein from the castor bean.

RNA (ribonucleic acid)
An organic acid polymer composed of adenosine, guanosine, cytidine and uridine ribonucleotides. The genetic material of some viruses, but more generally is the molecule, derived from DNA by transcription, that either carries information (messenger RNA), provides sub-cellular structure (ribosomal RNA), transports

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[225] NIH GHR.

[226] NIH MedlinePlus.

amino acids (transfer RNA), or facilitates the biochemical modification of itself or other RNA molecules.

Single Nucleotide Polymorphisms (SNP)[227]
A type of polymorphism involving variation of a single base pair. Scientists are studying how single nucleotide polymorphisms in the human genome correlate with disease, drug response, and other phenotypes.

Smallpox
See ‘Variola virus’.

Sonicator[228]
Sonicator is the instrument used to perform sonication. Sonication is the act of applying high-frequency sound waves to aid the dispersion of nanoparticles in a liquid.

Synthesis
The production of a substance by the union of chemical elements, groups, or simpler compounds or by the degradation of a complex compound (protein synthesis).

Synthetic Biology[229]
Synthetic biology is the engineering of biology: the synthesis of complex, biologically based (or inspired) systems, which display functions that do not exist in nature. This engineering perspective may be applied at all levels of the hierarchy of biological structures – from individual molecules to whole cells, tissues and organisms. In essence, synthetic biology will enable the design of ‘biological systems’ in a rational and systematic way.

Synthetic genomics
Synthetic genomics is a scientific discipline of synthetic biology related to the generation of organisms artificially using genetic material.

Taggant[230]
Generally, a taggant is a chemical or physical marker added to materials to allow various forms of testing. Specifically, it denotes a microscopic particle added

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[227] NIH GHR.

[228] Nanodictionary.

[229] European Commission. 2005. Synthetic Biology: Applying Engineering to Biology. Report of a NEST High-Level Expert Group, p. 5.

[230] Adapted from US Office of Technology Assessment. 1980. Taggants in Explosives. www.fas.org/ota/reports/8017.pdf.

to a commercial explosive in order to facilitate law enforcement, for example through identification of the batch of explosives, and the chain of legal distribution. Taggants of various kinds have also been used for identification and detection purposes not related to commercial explosives.

Thermocycler[231]
An instrument that repeatedly cycles through various temperatures required for an iterative, temperature-dependent chemical process such as the polymerase chain reaction.

Toxin
A compound produced by one organism, which is deleterious to the growth and/or survival of another organism of the same or different species.

Transfection
The infection of a cell with isolated viral DNA (or RNA), resulting in the production of intact viral particles.

Transformation
1. The uptake and integration of DNA in a cell, in which the introduced DNA is intended to change the phenotype of the recipient organism in a predictable manner. 2. The conversion, by various means, of cultured animal cells from controlled to uncontrolled cell growth, typically through infection with a tumour virus or transfection with an oncogene.

Transition
The substitution in DNA or RNA of one purine by another purine, or of one pyrimidine by another pyrimidine.

Transposition
The process whereby a transposon or insertion sequence inserts itself into a new site on the same or another DNA molecule. The exact mechanism is not fully understood and different transposons may transpose by different mechanisms. Transposition in bacteria does not require extensive DNA homology between the transposon and the target DNA.

Transposon
See ‘Transposition’.

Tropism (viral)
The ability of a virus to infect specific cell or tissue types

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[231] Nanoword, Encyclopedia Nanotech, www.nanoword.net/pages/encyclopedia.php.

Vaccine
A preparation of dead or attenuated (weakened) pathogens, or of derived antigenic determinants, that can induce the formation of antibodies in a host, and thereby produce host immunity against the pathogen.

Variola virus
Variola virus, a member of the orthopoxvirus family, is the cause of smallpox, an acute contagious disease. Variola virus is relatively stable in the natural environment. If aerosolized, it probably retains its infectivity for at least several hours if not exposed to sunlight or ultraviolet light. The variola virus has one of the largest viral genomes known.

Vector
1. An organism, usually an insect that carries and transmits pathogens. 2. A small DNA molecule (plasmid, virus, bacteriophage, artificial or cut DNA molecule) that can be used to deliver DNA into a cell. Vectors must be capable of being replicated and contain cloning sites for the introduction of foreign DNA.

Virion
A complete infectious virus particle.

Virulence
The degree of ability of an organism to cause disease. The relative infectiousness of a bacterium or virus, or its ability to overcome the resistance of the host metabolism.

Virus
A microscopic infectious agent that can only replicate itself in living cells of a host organism. It consists of a piece of nucleic acid - DNA or RNA - within a thin protein coat.

Zoonosis
Zoonosis refers to any disease or infection that is naturally transmissible from vertebrate animals to humans and vice-versa. They are caused by all types of agents: bacteria, parasites, fungi, viruses and unconventional agents.

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Abbreviations

AG	Australia Group
APHIS	US Animal and Plant Health Inspection Service
BAFA	German Federal Office of Economics and Export Control
BLAST	Basic Local Alignment Search Tool
bp	Base pairs
BW	Biological weapons
BWC	Biological Weapons Convention
BWC ISU	Biological Weapons Convention Implementation Support Unit
CBRN	Chemical, Biological, Radiological and Nuclear
CDC	US Center for Disease Control and Prevention
CNT	Carbon nanotube
CoC	Code of Conduct
CSIS	Center for Strategic and International Studies
CWC	Chemical Weapons Convention
DDBJ	DNA Data Bank of Japan
DG	Directorate General
DIY	Do-it-yourself
DNA	Deoxyribonucleic acid
EBI	European Bioinformatics Institute
EC	European Commission
EF	Edema factor
EMBL	European Molecular Biology Laboratory
EU	European Union
FBI	US Federal Bureau of Investigation
FSC	Forest Stewardship Council
HADDEX	Handbook of German Export Control
HHS	US Department of Health and Human Services
IAEA	International Atomic Energy Agency
IAP	InterAcademy Panel
IASB	International Association Synthetic Biology
ICRC	International Committee of the Red Cross
IfS	Instrument for Stability
iGEM	International Genetically Engineered Machine competition
IG DHS	Swiss Retailers Association
IGSC	International Gene Synthesis Consortium
INSDC	International Nucleotide Sequence Database Collaboration
ISN	US Institute for Soldier Nanotechnologies
ISU	BWC Implementation Support Unit
JCVI	J. Craig Venter Institute
LF	Lethal factor

MEMS	Micro-electromechanical systems
MIT	Massachusetts Institute of Technology
NBIC	Nanotechnology, Biotechnology, Information technology, Cognitive science
NCBI	US National Center for Biotechnology Information
NGO	Non-governmental organization
NIA	Nanotechnology Industries Association
nm	Nanometer
NPP	Non-pathogenic prions
NSABB	US National Science Advisory Board for Biosecurity
OFAC	US Office of Foreign Assets Control
OPCW	Organization for the Prohibition of Chemical Weapons
PA	Protective antigen
PCR	Polymerase chain reaction
POM	Polyoxometalate
PP	Pathogenic prions
RevCon	Review Conference
RIP	Ribosome inactivating proteins
RNA	Ribonucleic acid
ROS	Reactive oxygen species
SB2.0	Second International Meeting on Synthetic Biology
siRNA	Small interfering ribonucleic acid
SDN	US Specially Designated Nationals and Blocked Persons List
SNP	Single nucleotide polymorphism
ssDNA	Single-stranded DNA
TEGB	IASB Technical Expert Group on Biosecurity
UAV	Unmanned aerial vehicle
UN	United Nations
UNICRI	United Nations Interregional Crime and Justice Research Institute
UV	Ultraviolet
VIREP	Virulence Factor Information Repository
WMD	Weapons of Mass Destruction