Science and Technology and their Impacts on the Biological and Toxin Weapons Convention

A Synthesis Report on Preparing for the Seventh Review Conference and Future Challenges

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December 2011

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Executive summary

This study surveys important science and technology (S&T) trends relevant to the effective implementation of the 1972 Biological and Toxin Weapons Convention (BTWC), including in the context of the 2011 Seventh Review Conference. The amount of information on S&T activity is open-ended. It is nevertheless important to review major trends and methods (or approaches) that may be followed in order to understand the implications of S&T developments for biological arms control.

An attempt has been made to extend the type of sources and discussion often encountered in standard biological arms control analyses. It is hoped that this report provides a useful foundation for the further consideration of S&T developments, and methodologies for their assessment in the BTWC context.

The parties to the BTWC must recognize the implications of any paradigm shift emanating from S&T developments, both with respect to the prohibition of biological warfare and to the emergence of new framework conditions for scientific and economic cooperation and development.

Acknowledgements

The authors would like to thank those who assisted, supported or otherwise facilitated this project including: Dr Christer Ahlström, Dr Ian Anthony, Dr Volker Beck, Peter Bennett, Dr Gerrit Borchard, Dr Peter Clevestig, Ian Davies, Clara Ganslandt, Åsa Gustafsson, James Harrison, Ngoc Phuong Huynh, Dr Irene Kuiper, Milton Leitenberg, Richard Lennane, Ulf Lindell, Valentine Madojemu, Dr Lorna Miller, Dr Piers Millett, Ronnie Nilsson, Daniel Nord, Roger Roffey, Professor Steven Rose, Eva Schreuder, Rebecka Shirazi, Dr Katie Smallwood, Vincent Storimans, Dr Catherine Terry, Daniel Van Assche, Professor Olaf Wolkenhauer, Dr John R. Walker, Dr Robert A. Wampler and Dr Arthur Wolterink.

In addition, the authors would like to thank the following organizations: the British Foreign and Commonwealth Office (FCO), the Dutch Ministry for Foreign Affairs (MFA), the Netherlands Forensics Institute, the Implementation Support Unit (ISU), the Office of the President of the Seventh Review Conference to the BTWC, Codun, the Swedish Defence Research Establishment (FOI), the UK National Counter-Terrorism Security Office, and the Defence Science and Technology Laboratory (Dstl). Last, but not least, we would like to thank the Swedish MFA and the UK FCO for their generous support, guidance and expertise.

We would like to thank the SIPRI Editorial Department for its support. Any errors or omissions are the responsibility of the authors.

Abbreviations and acronyms

AG	Australia Group
BBSRC	Biotechnology and Biological Sciences Research Council
BGI	Beijing Genomics Institute
BTWC	Biological and Toxin Weapons Convention
BW	biological weapon/biological warfare
CBM	Confidence-Building Measure
CBW	chemical and biological weapons/chemical and biological warfare
Codun	EU Council Working Party on Global Disarmament and Arms Control
CoW	Committee of the Whole
CW	chemical weapon/chemical warfare
CWC	Chemical Weapons Convention
DHHS	Department of Health and Human Services
DoD	Department of Defense
Dstl	Defence Science and Technology Laboratory
EPSRC	Engineering and Physical Sciences Research Council
ESWI	European Scientific Working Group on Influenza
EU	European Union
FAS	Federation of American Scientists
FATF	Financial Action Task Force
FOI	Swedish Defence Research Agency
GERD	gross domestic expenditure on research and development
GPC	general purpose criterion
IASB	International Association [of] Synthetic Biology
ISRC	International Committee of the Red Cross
ICT	information and communication technology
IGSC	International Gene Synthesis Consortium
ISU	Implementation Support Unit
IUPAC	International Union of Pure and Applied Chemistry
KDD	Knowledge Discovery in Databases
LAI	laboratory acquired infection
MFA	Ministry for Foreign Affairs
MIT	Massachusetts Institute of Technology
MRC	Medical Research Council
NAIST	Nara Institute of Science and Technology
OECD	Organisation for Economic Co-operation and Development
OPCW	Organisation for the Prohibition of Chemical Weapons
PCT	Patent Co-operation Treaty
PSI	Proliferation Security Initiative
R&D	research and development
RCA	riot control agent
SAB	Scientific Advisory Board
SARS	severe acute respiratory syndrome

SIPRI	Stockholm International Peace Research Institute
SOP	standard operating procedure
S&T	science and technology
TBP	technology balance of payments
UK	United Kingdom
UN	United Nations
UNIDIR	United Nations Institute for Disarmament Research
UNODA	United Nations Office for Disarmament Affairs
USA	United States of America
VBM	valuable biological material
WHO	World Health Organization

1. Introduction

States continue to seek to identify and mitigate threats to their national security, including those posed by developments in science and technology (S&T) in the life sciences. This involves determining the security structure and resources necessary to meet perceived threats over the near- to longer-term. The formulation of national security policy is partly informed by the participation by states in regional and international security arrangements. S&T developments in the life sciences will continue to be considered in the chemical and biological weapon (CBW) arms control framework. This is particularly important as biology moves further from a descriptive to a predictive science.[1]

Biological and chemical weapons are prohibited by the 1972 Biological and Toxin and Weapons Convention (BTWC and the 1993 Chemical Weapons Convention (CWC). The BTWC member states must not 'develop, produce, stockpile or otherwise acquire or retain: 1. Microbial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes; 2. Weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict'.[2]

The convention thus embodies a general-purpose criterion (GPC) whereby all toxins (i.e. toxic chemicals of natural origin and their structural analogues and derivatives) and biological agents are prohibited unless for permitted purposes.[3] This is the mechanism by which new discoveries in S&T and possible future 'novel' agents are covered. Such agents may prove attractive for use in a variety of non-traditional conflicts which do not meet the standard definition of state-to-state war or where the intention may be to limit collateral casualties and deaths. The BTWC prohibits the development, acquisition, possession, transfer and (by implication) use of biological and toxin agents for 'hostile purposes', while the CWC prohibits the development, acquisition, possession, transfer and use of toxic chemicals and their precursors for weapons purposes.[4] The CWC also prohibits the use of riot control agents (RCAs) as a 'method of warfare'. Both conventions cover toxins. This double coverage of toxins may provide additional legal protections. However, this can also lead to situations where states decline to take specific measures to prevent the misuse of toxins as a chemical or biological weapon under either agreement.

As of December 2011 165 states were party to the BTWC.[5] The convention lacks a permanent institutional body to implement it. Negotiations on a legally binding protocol that would have created an international organization to implement the convention at the international level, including by conducting verification measures, failed in 2001. Since the end of the Fifth Review Conference in 2002, the member states have met annually to consider agenda items agreed by the preceding review conference. They have tabled numerous papers on various topics including national implementation, codes of conduct

[1] McLeish, C. and Trapp, R., 'The life sciences revolution and the BWC', *Nonproliferation Review*, vol. 18, no. 3 (Nov. 2011), p. 540.

[2] BTWC, article I.

[3] The GPC prohibits inter alia all toxins unless for permitted purposes.

[4] See Zanders, J. P., *The Prohibition of 'Use under the BTWC: Backgrounder on Relevant Developments During the Negotiations, 1969–1972* (BioWeapons Prevention Project: Geneva, 22 Nov. 2006).

[5] The states that have signed but not acceded to the BTWC are Central African Republic, Egypt, Guyana, Haiti, Ivory Coast, Liberia, Malawi, Myanmar, Nepal, Somalia, Syria and Tanzania. The states had neither signed nor acceded to the BTWC were: Andorra, Angola, Cameroon, Chad, Comoros, Djibouti, Eritrea, Guinea, Israel, Kiribati, Marshall Islands, Mauritania, Micronesia, Namibia, Nauru, Niue, Samoa, South Sudan and Tuvalu.

for scientists, biosafety, biosecurity and surveillance and response to disease outbreaks. The meetings, held in Geneva, have been facilitated by a temporary three-person Implementation Support Unit (ISU).[6]

National estimates on possible weapon activities traditionally fall within the purview of military establishments which generally have established procedures for determining their individual weapon-system requirements. Where a weapon system is prohibited under international law, as biological weapons are by the BTWC, the state's evaluation assessment dynamic is different. In this case, the weapon assessment becomes more a question of treaty verification, as well as threat assessments with regard to regime outsiders and scientific trends and political factors that could lead to treaty 'break-out' capabilities.

Schelling and Halperin characterize arms control to include 'all the forms of military cooperation between potential enemies in the interest of reducing the likelihood of war, its scope and violence if it occurs, and the political and economic costs of being prepared for it'.[7] They also state that arms control can be viewed 'as an effort, by some kind of reciprocity or cooperation without potential enemies, to minimize, to offset, to compensate or to deflate' certain characteristics of modern weaponry and military expectations, including an apparent perceived advantage accruing to the side that initiates a nuclear weapon strike.[8] Schelling and Halperin also argue that 'the essential feature' of arms control is 'the recognition of the common interest, of the possibility of reciprocation and cooperation even between potential enemies with respect to their military establishments'.[9]

Activities associated with arms control can, in principle, include: (*a*) reductions in some types of military force, (*b*) the enhancement of some types of military force, (*c*) qualitative weapon improvements, and (*d*) changes to methods of deployment and structures of military systems.[10] These factors were developed within the context of nuclear arms control during the cold war. Biological weapon arms control, on the other hand, has supported the development of a global disarmament regime under which all participating states forego completely (and permanently) the option of possessing and using a certain type of weaponry. While biological arms control was traditionally focused on the experience of large state-operated programmes, current threat perception is also driven by possible non-state actor threats and other risks associated with the diffusion of S&T and the impact of these developments and trends on security. Further, well-defined and focused S&T assessments and analyses of their methodologies that involve relevant national and international actors can assist to clarify further the nature and scope of such diffuse threats.

Many of the recent reviews of advances in S&T in the standard arms control literature remain descriptive. There is a lack of assessment of exactly what the impact of these advances on the BTWC regime could be. Many of the previous reviews illustrate the wide scope and fundamental nature of the change in the life sciences, but shy away from analysing how these developments may be applied for hostile purposes to affect human, animal and plant health through the physiological effects of biological agents and chemical substances. Such reviews have also avoided consideration of how these emerging possibilities affect some of the fundamentals of the BTWC regime, such as the relationship

[6] United Nations Office at Geneva, 'BWC Implementation Support Unit', <http://www.unog.ch/80256EE600585943/%28httpPages%29/16C37624830EDAE5C12572BC0044DFC1>.

[7] Schelling, T. C. and Halperin, M. H., *Strategy and Arms Control* (Twentieth Century Fund: New York, 1961), p. 2.

[8] Schelling and Halperin (note 7), p. 3.

[9] Schelling and Halperin (note 7), p. 2.

[10] Based on Schelling and Halperin (note 7), p. 2.

between defensive and offensive applications of biology, and the need to create transparency with regard to such developments (e.g. when applied in biodefence) and their impact on the verifiability of treaty compliance. The implications of developments in the life sciences and chemistry and their possible implications for the convention are continuing to evolve. There is a continuing need to reflect such implications and the associated main scientific trends in a manner that is policy relevant (in the context of the BTWC).

Four overarching questions for the BTWC Review Conference concerning S&T include:

1. What is an 'activity of concern' in the new S&T environment (and can one even usefully apply a concept of such 'activity of concern' in the dual-use context of the life sciences)?
2. What is the appropriate policy response with respect to both general S&T trends and developments and possible future specific activities that may require regulation and other governance responses? and
3. What is the expected operating environment of the BTWC over the coming 10–20 years?
4. Based on discusssions and consultations in 2011, it seems likely that an intersessional process will be agreed and that S&T will be reflected in the work programme. Whether and how should this topic be incorporated?

I. Project background

The present report is meant to provide input for policy options and common positions with a focus on the impact of S&T developments for maintaining the effectiveness of the convention in preparation for the 2011 BTWC Review Conference and subsequently. The project has been financially supported primarily by the Swedish Ministry for Foreign Affairs (MFA) with further support provided by the UK Foreign and Commonwealth Office (FCO). The authors would like to thank them for their generous support. On 5–6 March SIPRI convened a technical workshop to review and evaluate the impact of S&T developments on maintaining the effectiveness of the convention. It was attended by 17 researchers, scientists and officials. This paper partly reflects the presentations and the discussions from the seminar. A side presentation of the project was made at the meeting of the Preparatory Committee for the Seventh BTWC Review Conference in April.

II. Recent developments in the lead-up to Review Conference

During the lead up to the Seventh Review Conference many governments and senior officials have highlighted the need for S&T developments to be incorporated into future activity of the regime.[11]

The United States stated that it views the review conference 'as an opportunity to bolster' the convention, 'to take on the challenge of encouraging scientific progress, but constraining the potential misuse of science'.[12] The US representative went on to say 'We

[11] See ISU, 'Think zone for the Seventh Review Conference', <http://www.unog.ch/80256EE600585943/%28httpPages%29/BF4050089BB59EEDC12579300045A924 >.

[12] Gottemoeller, R., 'Remarks by Delegation of the United States of America First (Disarmament and International Security) Committee', United Nations General Assembly, New York, 4 Oct. 2011, <http://www.state.gov/t/avc/rls/175000.htm>.

will ask for member states to come together and focus on new ways to enhance confidence in compliance through richer transparency, more effective implementation, an improved set of confidence building measures, and cooperative use of the BWC's consultative provisions. We need to work together, moreover, on measures to counter the threat of bioterrorism, and to detect and respond effectively to an attack should one occur'.[13]

With regard to the impact of S&T developments, the USA has also drawn attention 'not only to developments with potential weapons application, but also to developments in diagnostics, countermeasures, and other areas that may mitigate the biological weapons threat. In addition to government experts, the participation of non-governmental stakeholders (including industry) should be sought, given the need for active engagement of these communities'.[14]

The European Union highlighted 'the vital importance of the Seventh Review Conference in deciding the future direction of this Convention'. And 'due to the rapid developments in science and technology (S&T) … encourages the States Parties at the Review Conference to consider a process of more frequent assessments of relevant S&T developments'. The EU also noted that 'more regular review could also serve to maintain a focus on the important role of S&T in the Convention'.[15]

India proposed that the review conference 'take a decision regarding structured and systematic review of S&T developments within the framework of the Convention. The aim is to build consensus among Member States based on a thorough review of developments in life sciences and biotechnology that are of relevance to the BWC, consistent with Article XII of the Convention'.[16]

President-designate of the review conference Ambassador Paul van den IJssel circulated a provisional indicative programme of work that envisages an article-by-article review of the convention by the Committee of the Whole (CoW) while informal plenaries will meet periodically to consider cross cutting issues.[17] In recent months Ambassador van den IJssel has facilitated open-ended consultations among the member states through informal meetings and communication on a third intersessional process that includes consideration of S&T.[18]

[13] Gottemoeller (note 12).

[14] USA, 'The next intersessional process', national paper submitted at Geneva, 2011, <www.unog.ch/80256EDD006B8954/%28httpAssets%29/FEFECBAFB08AACBBC12579430048E261/$file/US+working+paper+for+website.pdf>.

[15] EU, 'Preparation for the Seventh Review Conference of the States Parties to the Convention on the Prohibition of the development, production, and stockpiling of bacteriological (biological) and toxin weapons and on their destruction', EU statement submitted by Hungary, BWC/CONF.VII/PC/INF.2, 13 Apr. 2011, <www.opbw.org/rev_cons/prep_com/BWC_CONF.VII_PC_INF2_E.pdf>.

[16] India, 'Proposal for structured and systematic review of science and technology developments under the Convention', national paper submitted to BTWC states parties, 2011, p. 2, <www.opbw.org/rev_cons/prep_com>.

[17] Ambassador Paul van den IJssel, 'Letter to the Permanent Representatives of the States Parties and Signatories to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons Convention and on their Destruction', 17 Nov. 2011, <http://www.unog.ch/80256EE600585943/%28httpPages%29/87CF9BFD24A8D05FC1257574004B285B>.

[18] Ambassador Paul van den IJssel, 'Open-ended consultations on a new intersessional process', 18 Nov. 2011, <http://www.unog.ch/80256EE600585943/%28httpPages%29/ 87CF9BFD24A8D05FC1257574004B285B>.

2. The legal and political context

States operate in a variety of legal and regulatory environments at the national, regional and international levels. Some of the challenges associated with implementing higher-level political and overarching legal commitments have been highlighted in recent years as part of efforts to ensure the BTWC is fully implemented through state-to-state consultation, regional workshops and other actions.[19] Such activity is a process with no 'end point'. The parties to the BTWC can continue to consider how to extend the model of effective national implementation of the convention to relevant S&T monitoring and oversight, including in cases where economic cooperation and trade agreements exist. Finally, the parties might also wish to further consider how existing regulatory frameworks for dealing with substances that pose a health and safety, or security risk based on their pathogenicity or toxicity ought to be modified to include other existing or possible future risk factors. This could be carried out in the context of harmonization of national and regional regulations affecting human health and environmental safety.[20]

I. Regulatory issues

S&T issues are inextricably linked to regulatory frameworks, including EU legally binding instruments. The EU has three legally binding instruments: regulations, directives, and decisions. Regulations are immediately enforceable under national law. Directives specify what result should be achieved, but require member states to regulate how these results should be met within their respective jurisdictions. Decisions are binding on all legal persons or entities to which they are addressed.[21]

S&T regulatory frameworks should be evaluated in terms of a cost-benefit analysis of controls and oversight versus a 'bottom-up', more open system of governance and self regulation. To use a software analogy, will S&T evolve according to an open source free software collaborative model or will it follow a licensing-based fee paying model? Alternatively, will one see a mixture of the two, depending on how far certain activities in the life sciences have shifted from what is still essentially basic research, to the development of goods and services that are traded on the market (e.g. as is the case for medicines, tools and services in industry)? Some base research capacity may nevertheless be undermined because of an emphasis by many commercial financial backers on obtaining returns on investment over the near term. Although regulatory measures may be undermined by the pace of S&T advances or become progressively irrelevant in some respects, such measures and their associated frameworks will continue to exist for various reasons that are beneficial to society.

Robert H. Carlson represents the first understanding of the future of the life sciences when he argues:

'The broader revolution of distributed innovation, pervasive communication, and the fungibility of bits of atoms makes regulating access all the more likely to fail. The direct relevance of this

[19] For partial background, see e.g. Mathews, R. J., 'WMD arms control agreements in the post-September 11 security environment: part of the "counter-terrorism toolbox"', *Melbourne Journal of International Law*, vol. 8 (2007), pp. 292–310.

[20] See e.g. European Chemicals Agency, <http://echa.europa.eu/>.

[21] Discussion of the EU regulatory environment is partly based on Beck, V., 'The current European regulatory environment'. Presentation at SIPRI BTWC workshop, 5–6 Mar. 2011, Stockholm.

revolution to the biological technologies is that even if we attempted to regulate the parts of the DNA synthesizers or other equipment, rapid prototyping equipment and three-dimensional printers could be used to reproduce those components. In addition, prohibition is generally short lived and ineffective. Those arguing for attempting to improve safety and security through regulation and restriction must demonstrate successful examples of such policies within market economies. Front-end regulation will hinder the development of a thriving industry driven and supported by entrepreneurs and thereby engender a world that is less safe'.[22]

The parties to the BTWC at the previous intersessional process, on the other hand, took the view that there is value in inter alia: 'defining and implementing biosafety and biosecurity concepts in accordance with relevant national laws, regulations and policies' using such tools as 'accreditation, certification, audit or licensing for facilities, organizations or individuals; requirements for staff members to have appropriate training in biosafety and biosecurity; mechanisms to check qualifications, expertise and training of individuals'.[23]

One challenge for the Seventh Review Conference, and perhaps more so for the implementation mechanism (including any S&T monitoring and evaluation mechanism) that will emerge after its conclusion, will be to strike a balance that will not obstruct S&T progress while also creating sufficient regulatory strength at the level of national implementation (including, in the absence of international verification, accountability of government authorities) so as to ensure compliance by actors with the norm against biological warfare.

Here an examination of current financial incentives for R&D work could suggest effective oversight and compliance measures in the arms control context. Baskets of issues that could be considered in this context include achieving a better understanding of start-up financing and regulatory requirements and the manner in which the various actors in finance and industry normally interact. The role of governments and institutions to support commercialization of potentially sensitive S&T could also be further considered in the biological arms control context.

II. Compliance

The member states should consider further the extent to which the regime's original focus on traditional state-run biological warfare programmes might affect their understanding of possible future threats (this original focus has in fact been largely ignored or relegated to secondary status over the past eight years or so). At least three additional factors should be considered with respect to compliance: (*a*) non-state actor threats, (*b*) the implications of S&T developments for the non-BW production norm and (*c*) whether the concept of a 'BW agent' (i.e. a pathogen) can be reconciled with possible hostile intentions that entail causing the targeted promotion of the development of non-communicable diseases such as cancer in individuals and the like.

Background

Compliance can be phrased in terms of adherence to the norm (i.e. the absence of deliberate violations), or in terms of how effectively and comprehensively the parties are

[22] Carlson, R. H., *Biology is Technology: the Promise, Peril, and New Business of Engineering Life* (Harvard University Press: Cambridge, Mass., 2010), p. 239.

[23] 'Report of the Meeting of States Parties', BWC/MSP/2008/5, 12 Dec. 2008, para. 21.

implementing convention requirements. The former approach is focused on (perceived) state intentions as inferred from their activities (or lack thereof) and is potentially controversial and divisive. It can be managed in informal bilateral settings, or it requires a robust institutional framework if undertaken in a structured multilateral context. The latter approach (i.e. full and effective national implementation) is less problematic and can be managed reasonably well in a multilateral context. However, it carries the risk that discussions tend to shy away from addressing non-procedural-based implementation questions (including state activities that are open to different interpretations). Thus it is easier for the parties to consult on the status of regulatory frameworks and national implementing legislation, rather than on, for example, specific, biodefence research activity. The parameters of consultation on the capabilities and intentions of non-state actors may also be politically challenging.

The parties may wish to give further consideration to the process and mechanisms underlying any given compliance assessment, and to new opportunities emanating from advances in S&T. This allows, in principle, for a more focused technical consultation process. With respect to possible future allegations of biological weapon use, currently much more effective tools exist to support investigations of disease outbreaks and discriminate natural outbreaks from suspected use of a biological weapon.[24] As detection tools and methods develop, so does the potential for misdirection of forensics investigations. Globalization is also a factor that could facilitate such misdirection (or mischaracterization) in that emerging and re-emerging diseases make distinguishing natural from non-natural disease outbreaks more difficult.

As to means of routinely verifying treaty compliance, the bio-industry and associated research community have changed to a degree that previous concepts concerning routine site visits by international inspectors ought to be rethought through a fresh process of reviewing what information and activity are necessary to increase confidence in treaty compliance.

Allegations/suspicions that states fail to fully implement their international obligations to prevent biological (or chemical) warfare are likely to continue. Some of these allegations will also highlight the difficulty in distinguishing fundamental (i.e. deliberate, with the purpose of violating the norm) and 'technical' (i.e. innocent, caused by a lack of capacity or sufficiently attentive oversight) violations of international law and the possible role of a form of politicized legal dispute ('reductionism') that aims to cast aspersions on the behaviour of other states. In order to maintain the international prohibition against biological warfare, states and other interested actors should continue to consider relevant political and technical factors, such as a political inclination to wish to see preferred outcomes and how they relate to degrees of scientific certainty (or uncertainty) derived from such methods as sampling and analysis or the symptomatology of physiological effects of exposure to dangerous biological material where there is a suspicion that a biological agent has been deliberately employed for hostile (including covert) purposes or in armed conflict.

More broadly, current arms control and disarmament practice is as much concerned with state activities and deterrence as it is with coping with varied and diffuse groups of non-state actors, such as through oversight of the financial sector (i.e. to prevent or trace support for illicit activity), organized criminals and violent non-conformists and violent

[24] See Budowle, B., et al., *Microbial Forensics*, second. edn. (Academic Press: Burlington, MA, 2011). E.g. Murch, R. S. and Bahr, E. L., 'Validation of microbial forensics in scientific, legal, and policy contexts', pp. 649–663.

separatists.[25] It is also concerned with the application of non-proliferation measures, such as through the Financial Action Task Force (FATF), the G-8 Global Partnership Against the Spread of Weapons and Materials of Mass Destruction, the Proliferation Security Initiative (PSI) and UN Security Council Resolution 1540 (2004) (which amongst others requires states to adopt and enforce laws criminalizing acts by citizens or legal persons related to developing, acquiring, manufacturing, possessing, transporting, transferring or using nuclear, biological and chemical weapons and their means of delivery).

Another characteristic of arms control and disarmament in the post-cold war period is that strong states should perhaps show greater flexibility in their interaction with other states in order to agree common understandings and to mitigate shared security concerns. This dynamic is evident within multilateral arms control and disarmament regimes such as the CWC, and at the UN Office for Disarmament Affairs (UNODA). Areas of disagreement, such as the cross linkage of issues within and from outside the arms control context, must be managed in a constructive and sensitive manner. As such, states may agree general principles, while avoiding explicit discussion in the near term or they may consult informally at the margins of meetings only until the broader political situation develops in a manner that allows for a more formal understanding and agreement. It is therefore important to distinguish 'process' and 'results' with respect to the full implementation of any given treaty-based regime.

The BTWC policy processes need to be underpinned by thorough understandings (reviews) of the relevance and impact of advances in S&T on the regime. Possible structural elements for the consideration of S&T are provided below as well as in Annex A. The Seventh Review Conference could agree a process in which the parties, the research community, industry, academics, NGOs and civil society are able to exchange views and share information on the various methodologies and purposes for which S&T reviews have been undertaken. This consideration should also extend to a discussion of how the results of these reviews have been used in the practical implementation of BTWC requirements. As on previous occasions, space should be allowed at the margins of expert meetings of the parties in order to allow NGOs, civil society, industry and the scientific research community to make presentations and to table papers. This allows the parties to consider further how to identify the main relevant S&T developments and it would serve to promote longer term transparency and accountability in the context of the BTWC.[26] It may also help to inform consideration of how to maintain the prohibition against biological warfare (Articles I–IV) and its possible relevance to economic and technological development (Article X).

Such a process in an intersessional context could also have longer term political benefit by helping to elucidate the nature of what some perceive to be a fundamental dichotomy in the regime. Some argue that the value of the regime should be seen primarily in terms of its legal prohibition against biological warfare. Others emphasize that the full implementation of Article X is important to the day-to-day relevance of the regime. This is related to a broader discussion on the extent to which one article should be given greater weight than another where they seem to be incompatible in specific instances.

[25] Cooper, N. and Mutimer, D., 'Arms Control for the 21st Century: Controlling the Means of Violence', *Contemporary Security Policy*, vol. 32, no. 1 (Apr. 2011), p. 8.

[26] The understanding of 'transparency and accountability' is partly based on the analysis of Kjell Andersson. See Andersson, K., *Transparency and Accountability in Science and Politics: the Awareness Principle* (Palgrave Macmillan: Basingstoke, 2008), p. 102.

At the practical level of future work among the parties (including input from the ISU and external stakeholder communities—industry, research community, NGOs), it might be useful to solicit and collate a list of illustrative topics for studies relevant to S&T evaluation methodologies as part of an intersessional process. Working drafts could be collated and periodically circulated by the ISU.

Evaluation and transparency

In 2009 an academic working group summarized BTWC compliance mechanisms of Australia, Canada, Germany, the United Kingdom, and the United States.[27] The group observed that the review mechanisms for these states differ according to: (*a*) degree of formality, (*b*) whether they are used to evaluate individual projects, programmes or both, (*c*) the principal focus of the assessment, and (*d*) 'the degree to which independent oversight is exercised'.[28]

The meeting participants agreed that all the parties to the convention should have in place a compliance review process and communicate it to the other member states. The participants also observed that 'generating external legitimacy and confidence' requires more than having such a review process in place and that 'external observers' could, for example, 'weigh the context in which the process exists'.[29] The following elements or principles could be included in such a review process: (*a*) allowing external observers a role to 'weigh the context in which the process exists'; (*b*) determining whether the process 'is seen as encompassing all relevant activities, as existing within a respected rule of law, and as actually being followed'; and (*c*) achieving a better understanding on the degree to which states differ in their understanding of 'open and transparent'.[30]

The participants of the meeting also noted that complete transparency in biodefence activity is impossible to achieve.[31] Three major compliance review principles were posited and considered: (*a*) biodefence activity should be justified in terms of the provisions of the convention (either in terms of active evaluation or reactive evaluation), (*b*) that such activity should be both useful and critical for prophylactic, protective or other peaceful purposes and (*c*) a need exists for 'independent review and assessment of biodefense research and development activities'.[32] 'Critical' implies that the activity will provide significant (rather than marginal) benefit. The participants also discussed whether and how this consideration should be qualitative or quantitative (e.g. the nature and type of expenditure). Also related to the concept of criticality was the proposition 'that the development and production of a new pathogenic agent for threat assessments purposes' would be inconsistent with the convention if there is 'no credible evidence that any person or group has constructed such an agent'. Finally the participants emphasized the importance of ascertaining the context in which various biodefence-related activity is considered.[33]

[27] *Ensuring Compliance with the Biological Weapons Convention* (July 2009). Meeting Report sponsored by the Center for Arms Control and Non-Proliferation; Center for International and Security Studies at Maryland; Center for Science, Technology and Security Policy (American Association for the Advancement of Science); and Center for the Study of Weapons of Mass Destruction (US National Defense University) and held on 25 Feb. 2008 in Washington, DC.

[28] *Ensuring Compliance with the Biological Weapons Convention* (note 27), p. 16.

[29] *Ensuring Compliance with the Biological Weapons Convention* (note 27), p. 16.

[30] *Ensuring Compliance with the Biological Weapons Convention* (note 27), p. 16.

[31] *Ensuring Compliance with the Biological Weapons Convention* (note 27), p. 16.

[32] *Ensuring Compliance with the Biological Weapons Convention* (note 27), pp. 16–18.

[33] *Ensuring Compliance with the Biological Weapons Convention* (note 27), pp. 17–18.

A 1970 US policy evaluation from the US national archives shows how some biological threat activity proposed that year was deferred and one project disallowed on legal and ethical grounds. In particular, a proposal to disseminate the causative agent for rice blast into the environment was disallowed. The review also observed that 'alternative methods for testing required for biological threat analyses should be investigated'.[34]

Finally, specialized terminology used as part of the defence development and acquisition cycle may also provide insight into the appropriateness of a given activity or programme under the BTWC regime. For example, the Department of Defense (DoD) term 'critical path' is used to mean that the project will directly feed into a US conventional arms acquisition programme. The term could help to differentiate a S&T project that has potential weapon application versus one that does not.

Confidence-building measures

Several suggestions have been put forward for how to further advance the system of confidence-building measures (CBMs) under the BTWC. One is to move the system closer to a mandatory declaration system. Other proposals deal with the content of the submissions, the manner in which they are being used (reviewed, consulted, scrutinized) or whether they should all be made available to the public.[35]

In the context of compliance-related discussions and discussions related to S&T reviews, one further avenue could be to create new CBM formats dealing with issue areas that have not, as yet, been opened up for confidence building. For example, a politically-binding CBM template could be established to allow for the submission of S&T reviews currently undertaken at the national level in the life sciences in order to support risk assessments, as well as to identify needs in national biodefence. The focus should be on achieving a greater understanding of the S&T evaluation methodology employed, rather than attempting a comprehensive listing of the activities evaluated or the associated results.

[34] Memorandum for the Chairman, Joint Chiefs of Staff, Subject: 'Deseret Test Center FY 1970 Chemical-Biological Joint Operational Test Program (U)', 18 Feb. 1970. Ford Presidential Library. Declassified 31 Aug. 2011. At the time the Defense Research & Engineering was headed by John S. Foster (1 Oct. 1965-21 June 1973). Source: 'A history of the Office of the Director of Defense Research and Engineering', <http://www.dod.gov/ddre/ddre_history.htm>.

The authors are grateful to Milton Leitenberg of the University of Maryland and Robert A. Wampler of the US National Security Archive for drawing their attention to this recently released document and for sharing their insight on its importance.

[35] Much of this work has been carried out by the Hamburg University Research Group for Biological Arms Control. See 'Improving the confidence building measures under the BWC', <http://www.biological-arms-control.org/projects_improvingthecbms.html>. The topic is also periodically raised in various national papers.

3. Science and technology developments

States have long considered S&T in terms of both their own security requirements and the potential military capabilities of other states.[36] Such assessments increasingly take into account the capabilities and intentions of non-state actors, including those known to have hostile or violent intentions.

The parties to the BTWC might wish to consider further the relevance of how such S&T assessments have or could be carried out in the national and international peace and security contexts (see table 3.1)

Table 3.1. Overview of S&T developments

General trends
Convergence
Increasing understanding of the life processes and the functioning of biological systems
Trends in biotechnology
Global distribution of life science capacity
Open science
Media, perception and society
Developments with possible negative consequences
Specific research and projects of interest
Advances with potential for weapon applications
Improved understanding of toxicity, transmission, infectivity, virulence and pathogenicity
Enhancing a biological weapon agent (e.g. selectivity, enhanced targeting, stability)
Producing biological weapon agents
Circumventing existing control mechanisms
Neurobiology (new types of biological agents and toxins)
Developments with possible beneficial consequences
Detection
Diagnostics
Prevention, prophylaxis and vaccination
Therapeutics
Response capacity
Enabling advances and technologies
Characterizing biological systems and networks
Manipulating biological systems and networks
Engineering biological systems and networks
Gathering and manipulating biological information
Converting biological information to digital data and back
Generic enabling technologies

Source: With minor modifications, based on ISU, 'New scientific and technological developments relevant to the Convention: background information document submitted by the Implementation Support Unit', undated.

[36] E.g. Kostoff, R. N., et al., *The Structure and Infrastructure of Chinese Science and Technology* (Office of Naval Research: Arlington, VA, 2006), unclassified; Kostoff, R. N., *Structure of the Anthrax Research Literature* (Office of Naval Research: Arlington, VA, 2006), unclassified; Kostoff, R. N., Koytcheff, R. and Lau C. G. Y., *Structure of the Global Nanoscience and Nanotechnology Research Literature* (Office of Naval Research: Arlington, VA, 2006) unclassified; and Glotzer, S. C., et al., *International Assessment of Research and Development in Simulation-Based Engineering and Science*, World Technology Evaluation Center Panel Report (WTEC, Inc.: Baltimore, Maryland, 2009), unclassified.

I. S&T evaluation approaches

Many existing security and defence evaluation methodologies are outside the arms control and disarmament context (although during the cold war this was less true as compared to the present). Nevertheless, it may be useful to review some of the broader contexts in which such methodologies have been developed and applied. Hans Günther Brauch has observed: 'The relationship of military technology, stability and arms control has been a persistent theme of the strategic debate' and stresses the importance for international arms control agreements to 'cope with military technology and contain the technological momentum'.[37]

A state's technology base may face a variety of political, economic and ideological structural constraints such as an inability to transfer civilian research for military applications, a focus on import substitution to acquire technology, poor planning and various inefficiencies arising from bureaucratic constraints.[38]

Research may typically be carried out at university, private industry or in military service facilities. Indicators of activity for national security and defence purposes could include: (*a*) the ratio of civilian to military personnel at a given facility overall, and in the management structure, (*b*) the existence and level of security classifications, (*c*) whether research is published or abstracts of the work is published, (*d*) the number and type of disciplinary measures taken at a given facility or in a given sector, (*e*) whether the defence R&D objectives and funding (type and amount) are published, (*f*) whether researchers from defence establishments are allowed to participate in international conferences and publish scientific work and (*g*) whether defence research establishments host open international research conferences and symposia. In addition, various S&T indicators may provide 'granularity' to the direction and significance of activity such as the ratio of research funding to total R&D funding.

Generic S&T challenges include maintaining longer term financial commitments for uncertain future benefits, ensuring appropriate continuity of support mechanisms, and ensuring that oversight and reporting requirements do not unduly inhibit the project goals.

An improved broader understanding of differences among states' defence and security priorities and activity may help to provide context to the question of how to better understand BTWC compliance-related matters. For example, some states have legal, political, organizational and, perhaps, cultural barriers to allowing the accessing of base research for defence acquisition and development. Japan, for example, has many dual-purpose technologies in its commercial technology base. However, the country has 'firewalls' that inhibit or prevent transfers from civilian companies to the military.[39] In addition, many in the public (including in civilian companies) simply wish to avoid contact with the Japanese military.[40] Nevertheless, corporations may, to varying degrees, be motivated or influenced by financial interests and necessity, rather than by national security interests or by multilateral peace and security policy developments.

[37] Brauch, H. G., 'Military technology—armaments dynamics—strategic stability implications for arms control and disarmament', pp. 20, 25 in Ed. Hans Günther Brauch, *Military Technology, Armaments Dynamics and Disarmament: ABC Weapons, Military Use of Nuclear Energy and of Outer Space and Implications for International Law* (Macmillan Press: Basingstoke, 1989).

[38] E.g. Arnett, E., 'Beyond threat perception: assessing military capacity and reducing the risk of war in southern Asia', p. 9 in Ed. Eric Arnett, *Military Capacity and the Risk of War: China, India, Pakistan and Iran* (Oxford University Press: Oxford 1997).

[39] This discussion concerns conventional armaments.

[40] This is analysis of conventional weapons acquisition and development only.

The US Defense Science Board Task Force has periodically evaluated DoD S&T requirements. One found that while the 'optimum level of DoD investment in science and technology' cannot be agreed, most successful industries invest approximately 15 per cent of sales profits in R&D and that private sector 'research' is equivalent to DoD's 'S&T'.[41] In 1998 the DoD and Service S&T Program was carried out by universities (10 per cent), university affiliated research centres (25 per cent), industry (45 per cent) and 'service laboratories' (20 per cent).[42]

The same year the US board also concluded that 'no formulas for establishing S&T funding have been discovered in government agencies or in industry. An analytic framework for establishing R&D funding can be formulated, but the coefficients of the equation terms are not known at this time'.[43] The board was unable to determine whether any formula exists in either government or industry which 'could be applied to answer the question of setting the level' of S&T investment.[44] The group's methodology relied heavily on a survey of only 12 major US corporations. Partly on this basis, the board concluded that there was a 'fairly universal subjective approach' to setting the investment levels which consisted of the Chief Executive Officer, the Chief Financial Officer, the Chief Technology Officer and one or two other invitees who would decide the levels of R&D investment.[45] Private industry R&D interest is principally one of economic gain, while a government's R&D interest is to promote longer term economic prosperity and its national security.[46] Government contractors (including corporations) that pursue R&D projects may have interests more in line with those of government agencies, rather than private industry. The board found that one-third of US corporate R&D spending was exploratory and focused on 'revolutionary technologies', while the balance was focused on 'evolutionary improvements in identified product needs'.[47]

A longstanding difficulty in transforming base research and development is the transfer to the weapons acquisition cycle. This transition requires established procedures that form an 'acquisition path' whereby technology can be taken from the research facility context to the weapons acquisition pathways.[48] At least at the national level, states may continue to consider the significance of the basic structure and operating procedure of weapon acquisition pathways and whether any other (perhaps classified) pathways are in place for 'special' (or equivalent) research programmes.

Threat perceptions—contemporary and historical—are also useful to consider in an S&T defence and security (including arms control) context. A past study on Soviet military technological challenges issued by a panel of US academics and government officials characterized the then Soviet chemical and biological warfare threat as follows:

'The Soviet Union has a substantial chemical warfare capability in its army units. Both the United States and the Soviet Union have long been interested in biological agents and vaccine defenses against them. The United States is demonstrating in Vietnam that defoliants and anticrop chemicals can be effective. There is room for considerable improvement in such areas of chemical and

[41] *Report of the Defense Science Board Task Force on Defense Science and Technology Base for the 21st Century* (Office of the Under Secretary of Defense for Acquisition & Technology: Washington, DC, June 1998), p. 3.
[42] *Report of the Defense Science Board Task Force* (note 41), p. 4.
[43] *Report of the Defense Science Board Task Force* (note 41), p. 21.
[44] *Report of the Defense Science Board Task Force* (note 41), p. 14.
[45] *Report of the Defense Science Board Task Force* (note 41), p. 14.
[46] *Report of the Defense Science Board Task Force* (note 41), p. 14.
[47] *Report of the Defense Science Board Task Force* (note 41), p. 22.
[48] *Report of the Defense Science Board Task Force* (note 41), p. 25.

biological warfare as nonlethal and incapacitating agents, antipersonnel chemicals and antichemical agents and lethal types of agents.

A strong attitude exists in the United States that escalation from use of nonlethal to lethal chemical and biological agents could too easily occur, and hence that the United States should not develop them. No such attitude toward research and development in chemical and biological warfare, however, has been manifested in the Soviet Union. To the contrary, the Soviets have maintained an aggressive program and have conducted maneuvers which simulated defense against biological and chemical agents. They seem to have permitted the Egyptians to use chemicals in the Yemen war, and might have done the same in the Israeli conflict if reports that the Egyptians had large stocks of chemical agents for use against the Israelis are true'.[49]

This panel outlined the difficulties faced by US policy makers when attempting to ensure that Soviet S&T developments did not give the Soviet Union an advantage as follows:

'To pursue the potential military application of each and every promising scientific and technological theory or development within the adversary's capability would be impossible [for the United States], but to limit oneself only to those that one believes the potential enemy might find attractive would be too risky. To escape from the dilemma the policy maker must put priority on long lead time items in the most important fields, carefully considering the risks of delay and faulty decision making. At the same time, he must continue to build an expanding base of technology that can both advance our own capabilities for new systems and reduce reaction time when a new weapon actually appears in the arsenal of the potential enemy. He must constantly look for military applications the potential enemy may not have recognized or may have failed to pursue. All of these investments must be compared against the expected value of other investments in new intelligence systems that might increase our warning time concerning progress on the other side'.[50]

Finally, the manner in which patents are evaluated and granted could be considered in terms of their potential relevance to biological arms control.[51]

S&T evaluation in the economic development context

The Organisation for Economic Co-operation and Development (OECD) has been collecting research and development (R&D) data on its members since the early 1960s and on some non-member states since the 1990s in an attempt to characterize the associated R&D levels and trends.[52] The standard expenditure measure employed by the OECD is the Gross Domestic Expenditure on Research and Development (GERD).

The OECD also attempts to measure indirectly the output and impact of S&T.[53] Three proxy indicators for the output and impact of S&T include (*a*) patents, (*b*) the technology balance of payments (TBP) and (*c*) 'trade in R&D intensive industries'.[54] Information on patents indicate the level, scale and type of inventions (e.g. total number, national percentages of triadic patent families).[55]

[49] Center for Strategic Studies, *The Soviet Military Technological Challenge*, Special Report series no. 6 (Georgetown University: Washington, DC, Sep. 1967), p. 76.

[50] (note 49), p. 96.

[51] E.g. for information on the US DoD's 'patent security review process', see DoD, Directive no. 5535.02, 24 Mar. 2010. This activity is partly based on the US Invention Secrecy Act of 1951.

[52] OECD, *Main Science and Technology Indicators*, no. 1 (OECD: Paris, 2011), p. 3.

[53] OECD (note 52), p. 4.

[54] OECD (note 52), p. 4.

[55] OECD (note 52), p. 4

The OECD extracts TBP data from national sources (i.e. balance of payments and survey results) in an attempt to measure the flows of technological 'know-how' and services.[56] The OECD's methodology for compiling TBP is contained in its manual *Proposed Standard Method of Compiling and Interpreting Technology Balance of Payments Data* (1990).[57] TBP data consist of 'money paid or received for the acquisition or use of patents, licenses, trademarks, designs, inventions, know-how and closely related technical services'.[58]

The OECD also observes that 'indicators of trade performance in R&D intensive industries can be used as proxy measures of the industrial and economic impact of scientific and technological activity'.[59] The organization compiles tables providing the trade balances and export market shares in five R&D intensive fields: (*a*) aerospace, (*b*) electronics, (*c*) office machinery and computers, (*d*) pharmaceuticals and (*e*) instruments.[60] These categories may not reflect the current and future trajectory of S&T developments. Perhaps the most relevant OECD categories for biological arms control and S&T evaluation and oversight in the life sciences are the data that cover computers, pharmaceuticals and instruments.

The body obtains some of its patent data from the applications filed under the Patent Co-operation Treaty (PCT) with a focus on those patents in the fields of information and communication technology (ICT) and biotechnology.[61]

Finally, OECD data on R&D typically cover both the natural sciences (including agriculture and the medical sciences) and engineering.[62] Many countries collect data on R&D activity in the Business Enterprise sector of engineering only.[63]

S&T and the understanding of disease

The understanding of disease and integration of base and applied research to treat disease continues to develop. The parties to the convention may wish to further evaluate the resulting implications for the BTWC regime. For example, physicians traditionally base their diagnoses on the *International Classification of Diseases* which was established about 100 years ago. However, in November 2011 the US National Research Council released a study that argues that classifying disease according to various molecular pathways would be more effective for several reasons, including the fact that it would facilitate the sharing of information among scientists who study the same molecular structures (but different diseases).[64] A major goal of the group is to more effectively connect clinical (including personal patient) information and research data. The report's authors wish to reduce health care costs partly by facilitating the taking of broad research findings and individualizing their implications for patients through an information network called the *Information Commons and Knowledge Network*. Doctors would then be able to obtain a better understanding of the current and likely health outcomes of treatments based on the

[56] OECD (note 52), pp. 4–5.
[57] OECD (note 52), p. 5.
[58] OECD (note 52), p. 5.
[59] OECD (note 52), p. 5.
[60] OECD (note 52), p. 5.
[61] OECD (note 52), p. 4
[62] OECD (note 52), p. 103.
[63] OECD (note 52), p. 103.
[64] Committee on a Framework for Developing a New Taxonomy of Disease, *Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease* (National Research Council: National Academies Press: Washington, DC, 2011). Prepublication copy.

patient's particular life habits and genetic predispositions. The report also calls for harmonizing the taxonomies that inform medical education, biomedical research and disease coding systems. Information concerning the health of patients include their microbiome, epigenome, genome, signs and symptoms and exposome.[65]

The US National Research Council also observes that biology has become a 'data-intensive science' as exemplified by the rise of DNA sequencing technology. The GenBank, as of 2011, has more than 300 billion base pairs.[66] As of January 2011 the cost of carrying out a complete genome sequence was estimated to be approximately $(US)21 000 and this cost is expected to drop to approximately $(US)1 000 within several years.[67] According to another estimate, the cost of sequencing a single human genome cost $(US)8.9 million in July 2007 and approximately $(US)10 500 in July 2011.[68] Within the 12 months or so, the cost of sequencing an individual's DNA is expected to drop below $(US)1 000.[69]

The current international DNA sequencing capacity is estimated to be 13 quadrillion base pairs per year. BGI, formerly known as the Beijing Genomics Institute, is reportedly the world's largest genomic research institute. It posseses 167 DNA sequencers which generate the equivalent of approximately 2 0000 human genomes per day (a human genome contains approximately 3 billion base pairs).[70]

The principal bottleneck with respect to DNA sequencing is the ability of scientists and others to analyse the huge explosion of data. Unlike most other data intensive sciences, such as astronomy and physics, actors in the life sciences are more numerous, decentralized and widespread. DNA sequencing, in turn, is only partly responsible for this explosion. Scientists are generating even more data on RNA, proteins and bio-chemistry of cellular and intra-cellular processes.[71]

Finally, the US National Research Council has observed that human physiology is 'far more complex than any known machine' and that the 'molecular idiosyncrasies' of individuals present 'exhilarating potential and daunting challenges' in attempts to achieve 'personalized medicine'.[72] Of the millions of sites where individuals' genomes differ, over 10 000 of the differences are currently 'known to have the potential to alter physiology'.[73]

S&T in the BTWC context

S&T developments can be considered in at least three respects with regard to the implementation of the convention: (*a*) ensuring that the prohibitions against biological warfare are effectively maintained (Article I), (*b*) identifying areas of life sciences and technological development that require regulatory or other governance measures to manage associated risks (Article IV), and (*c*) economic and technological development (Article X).

Prior S&T evaluation methodologies and results have included:

[65] Committee on a Framework for Developing a New Taxonomy of Disease (note 64), p. 15.
[66] Committee on a Framework for Developing a New Taxonomy of Disease (note 64), pp. 19–20.
[67] Committee on a Framework for Developing a New Taxonomy of Disease (note 64), p. 20.
[68] Pollack, A., 'DNA researchers' data deluge', 2 Dec. 2011, *International Herald Tribune*, p. 16.
[69] Pollack (note 68), p. 16.
[70] Pollack (note 68), p. 16.
[71] Pollack (note 68), p. 16.
[72] Committee on a Framework for Developing a New Taxonomy of Disease (note 64), p. 21.
[73] Committee on a Framework for Developing a New Taxonomy of Disease (note 64), p. 21.

(*a*) reviews by individual States Parties (in the early years by the depositories)—these are often issue-focused and selective;
(*b*) reviews compiled on request by the ISU;
(*c*) reviews by the Review Conference itself (a fairly limited process by time and somewhat pre-determined by what emerges in the papers submitted by member states, as well as the background papers compiled by the ISU); and
(*d*) external input by relevant scientific bodies, industry and other NGOs.

A number of points should perhaps be explicitly stated. The first is actors are involved in following implementation of the BTWC in capitals. These broadly fall under the following categories: (*a*) the political and diplomatic community, (*b*) defence establishments, (*c*) the scientific research community, and (*d*) industry.

Any intersessional process to assess S&T should pay due attention to the perspectives and activities of all these actors. The formulation and implementation of science policy advice is also of continuing importance, including for supporting informed decision making by the higher-level leadership. The Federation of American Scientists (FAS) has observed, for example, that 'While technical analysis is almost never sufficient to make wise choices, absent competent, timely, targeted scientific and technical analysis, these decisions will depend on unchallenged assertions by special interests and ideologues'.[74]

For the purposes of the Seventh Review Conference, the consideration of the S&T developments ought to be structured in a meaningful and functional manner for the diplomatic community. This should be done separately for the higher-level political leadership, as the two communities are distinct from each other. The scope of S&T should be representative of trends in the field and directly relevant to the implementation of the convention. Otherwise, consideration of S&T could become too diffuse: consisting of everything and nothing, or consisting of a 'data dump' of processes, meetings and research results. The level of detail concerning S&T should also be relevant from a policy perspective, including the full and effective implementation of the BTWC. Criteria for treaty relevance could include:

(*a*) discovery of new types of biological or toxin agents (including synthetic analogues and derivatives of naturally-occurring agents) that might be relevant for biowarfare;
(*b*) new understandings of the functioning of biological processes/systems that might lead to the design of new/different types of biological warfare agents;
(*c*) new discoveries and understandings that could lead to better protection against biological weapons and toxin agents and treatments for those exposed to them;
(*d*) S&T advances that may be useful in investigations of alleged non-compliance including biological weapon use;
(*e*) developments that affect transparency among the parties with regard to new directions in biological R&D, including biodefence; and
(*f*) developments that create new opportunities or conditions for the promotion of international cooperation in the life sciences.

Models exist for defining and implementing policies (mainly at the national level) for assessing S&T trends. This has been carried out in order to promote or develop a sufficient scientific national research and development base, mainly for economic development and for national security purposes. Threat perceptions are informed by the capacity of states to

[74] Kelly, H., et al., *Flying Blind: the Rise, Fall, and Possible Resurrection of Science Policy Advice in the United States*, occasional paper no. 2 (FAS: Washington, DC, Dec. 2004), p. 1.

understand the capabilities and intentions of other actors (e.g. potential opponents), including the effects of developments in S&T to collect and understand the activities of such opponents.[75] To maintain this capacity, some states have periodically considered the extent to which S&T developments internationally might affect their ability to detect and understand possible threats, including biological ones.

The following sections consider in some detail five areas of research into the life sciences and related enabling technologies that have been selected for this project because of their relevance to the BTWC. These include synthetic biology (including synthetic genomics), systems biology and bioinformatics, brain research, targeted drug delivery, and bioforensics. Other fields are naturally relevant and, to an extent, the areas selected merely serve to illustrate the more fundamental underlying S&T trends. A rationale nevertheless exists for selecting these areas.

The principal reason for including synthetic biology (as well as systems biology/bioinformatics) is that it is an evolving discipline at the intersection of previously separate research activity. Any such convergence in the sciences has the potential for bringing about new opportunities and approaches for international cooperation and can lead to unexpected scientific discoveries. Such discoveries are inherently unpredictable and can result in beneficial applications and create new risks. Therefore such research will require careful monitoring with an ability to take decisions on risk management if and when needed.

Brain research is another interdisciplinary field that is experiencing rapid development and will lead to new and better understanding about the functioning of the human brain and its biochemistry. This could result in a vast range of new applications in medicine and disease treatment, as well as new military or defence applications (e.g. for performance enhancement and man–machine interfaces). However, such developments also allow for the development of chemical and biological agents with novel toxicological profiles that might change assessments on the utility (or lack thereof) of CBW. For example, there is a risk that incapacitating agents could be introduced for law enforcement and certain types of combat operations that require 'less-than-lethal' weapon principles.[76]

Targeted drug delivery is a field that affects both the ability to treat disease in a more selective and efficient manner that results in fewer side effects, and has potential utility to deliver more efficiently biological agents for weapon purposes. In the context of biological weapon risk assessment, developments in targeted drug delivery can change the underlying context for such evaluations. The type of molecules that, under traditional assessments, possessed little or no weapon utility in view of their bio-chemical and physiological properties, could prove to be more attractive as weapon agents if current or future drug delivery techniques are utilised. For example, the utility of bioregulators have been frequently cited in the literature as potential agents for use for hostile purposes.[77]

Finally, advances in bioforensics have changed some of the understanding by security analysts regarding the ability to discriminate between natural disease outbreaks and deliberate agent releases. This will affect the ability by states and other actors to verify the

[75] Intelligence Science Board, Task Force Report on the Intelligence Community and Science and Technology, *The Challenge of the New S&T Landscape* (Office of the Director of National Intelligence: Washington, DC, Nov. 2006) . Partially declassified 2010.

[76] See e.g. Sutherland, R., *Chemical and Biochemical Non-lethal Weapons: Political and Technical Aspects*, SIPRI policy paper no. 23 (Nov. 2008).

[77] E.g. Tucker, J., 'The body's own bioweapons', *Bulletin of the Atomic Scientists*, no. 64, no. 1 (Mar./Apr. 2008), pp. 16–22.

BTWC especially (but not exclusively) with regard to investigations of the alleged use of biological or toxin weapons.

II. Synthetic biology (including synthetic genomics)

There are at least two main ways to understand synthetic biology. [78] One is that it aims to synthesize 'biological structures or life forms in the laboratory that do not exist in nature', while the other emphasizes a chemical approach in which the goal is to synthesize 'molecular structures and/or multi-molecular organized biological systems that do not exist in nature' and which may be obtained through either chemical or biochemical syntheses.[79] Pier Luigi Luisi characterizes this dichotomy as 'the two souls of synthetic biology'. Under the former approach, the purpose is defined a priori and an engineering-type solution is sought. Under the second approach, the research problem is structured by posing the question 'why this and not that'? Luisi illustrates the latter approach with the following examples: 'Why did nature do things in a certain way, and not in another one? Why 20 amino acids, and not 15 or 55?'.[80]

Synthetic biology may also be said to consist of several subfields including: (*a*) DNA synthesis, (*b*) DNA-based biological circuits, (*c*) the 'minimal genome', (*d*) protocells and (*e*) xenobiology.[81] More broadly, synthetic genomics essentially entails the recreation or de novo synthesis of genes and/or whole genomes. Synthetic biology aims at the deliberate design of novel biological systems and organisms, drawing on principles elucidated by biologists, chemists, physicists and engineers.[82]

Synthetic genomics and synthetic biology open up cross-disciplinary possibilities—the full scope of which remains uncertain. For example, in the near future one need not necessarily be trained as a microbiologist in order to apply synthetic biology within alternate fields. This also creates the possibility of the often cited 'garage science' in the life sciences which will, in turn, be a generally positive development to drive innovation. However, such work also carries some potential safety and security risks. A somewhat similar scenario was the development and spread of computer programming in society in the 1980s and 1990s. Although individuals are unlikely to master the synthesis of a working pathogen at home (let alone the development of an effective dissemination device), they may be able to create material that poses a distinct safety hazard, under

[78] Possible understandings of synthetic biology include: (*a*) biocircuits using standard biological parts, (*b*) biocircuits without standard biological parts , (*c*) engineering cells to produce fine chemicals, (*d*) creating artificial life, (*e*) computer software for biocircuit design, (*f*) artificial ecosystems, (*g*) enlarged genetic alphabet, (*h*) DNA with chemically different backbone, (*i*) minimal genome and (*j*) understanding the origin of life. Pei, L., Gaisser, S. and Schmidt, M., 'Synthesis biology in the view of European funding organisations', *Public Understanding of Science*, vol. 1 (2011), p. 5.

[79] Luisi, P. L., 'Introduction', p. 1 in Eds. Pier Luigi Luisi and Cristiano Chiarabelli, *Chemical Synthetic Biology* (John Wiley: Chichester, 2011).

[80] Luisi, P. L., 'The synthetic approach in biology: epistemological notes for synthetic biology', pp. 343–362, in Eds. Pier Luigi Luisi and Cristiano Chiarabelli, *Chemical Synthetic Biology* (John Wiley & Sons, Ltd.: Chichester, 2011).

[81] Schmidt, M. and Pei, L., 'Synthetic toxicology: where engineering meets biology and toxicology', *Toxicological Sciences*, vol. 120 (2010), p. S208. The prefix xeno- is not exclusive to items or organisms of extra-terrestrial origin. For e.g. it can be used to denote 'between species' and is commonly found in discussions concerning organ transplants. The World Health Organization (WHO) 2006 *Laboratory Biosecurity Guidance* states that valuable biological material (VBM) may include 'biological/geological samples taken from other planets and transported to Earth. The uniqueness of such agents or samples, the potential health and biological risks their release represents, are compelling reasons for them to be safeguarded, protected, accounted for and appropriately secured'. *Biorisk Management: Laboratory Biosecurity Guidance* (WHO: Geneva, Sep. 2006), p. 18. 'Xeno' should be understood to mean anything 'not natural' in the synthetic biology context.

[82] The Royal Society, *Synthetic Biology—Discussion Meeting Summary*, Scientific discussion meeting (Royal Society: UK, Aug. 2008).

conditions which are less than optimal under current standard practice to handle such hazards.

The current security concern over synthetic genomics relates mainly to industry products and associated production capacity which, in turn, can be ordered on the Internet. Oversight mechanisms include the development of databases that contain 'red flags' that might indicate a suspicious order. Many companies, for example, will not make deliveries of DNA sequences or genomes to residential addresses. Some DNA sequences are deemed 'sensitive' under guidelines being developed by the USA and others. In 2009 the US Department of Health and Human Services (DHHS) issued draft guidance in this area. As already mentioned, the extent to which such guidelines might be effective remains uncertain.

Of particular interest for the S&T review are areas where sudden and unexpected changes may occur. For example, in 2010 the US *Presidential Commission for the Study of Bioethical Issues* observed that although agents generated through synthetic biology are 'unlikely to raise novel risk assessment or risk management issues', one of the biggest oversight challenges for synthetic biology is the science's 'capacity to create novel entities that are increasingly dissimilar to known agents or organisms, making potential risks harder to assess'.[83] Such uncertainty often emerges where science moves into new fields of investigation, and/or where different branches of S&T are brought together to investigate common problems.

In the life science context, such 'convergent technologies' have been defined as 'the combination of four major scientific and technological fields: (1) nanotechnology, (2) biotechnology, including genetic engineering, (3) information technology, and (4) cognitive science, including cognitive neuroscience'.[84] However, this definition focuses on cognition and neuroscience. It can be argued that similar 'convergence areas' may be described with respect to biological, biochemical and chemical processes (e.g. chemical production by synthesis involving biological or biologically mediated methods).[85] Various other convergence paradigms are also possible and present a distinct field of inquiry.

Developments

Biologial arms control and security analysts commonly refer to certain examples of research 'of concern' including: the reconstruction of the genome of the poliovirus, the reconstruction of the genome of the 1918 strain of influenza, the design of a synthetic SARS-like coronavirus and the creation of a bacterial cell that was controlled by a chemically-synthesized genome. DNA sequencing and the recreation of 'historical' or 'novel' pathogen strains are of continuing interest and possible concern in connection with ensuring BTWC compliance. DNA recovery and sequencing from 'ancient' specimens are increasingly feasible. This provides greater insight into the function of pathogens and the nature of associated virulence factors. For example, in 2005 scientists from the US Armed Forces Institute of Pathology in Rockville, Maryland, published the full sequence of the influenza strain responsible for the Spanish flu pandemic of 1918 (estimated to have killed up to 50–100 million people), which was extracted from infected tissue obtained from the

[83] Presidential Commission for the Study of Bioethical Issues, *New Directions: the Ethics of Synthetic Biology and Emerging Technologies* (Washington, DC, Dec. 2010), p. 83. See also, Endy, D., et al, 'Adventures in synthetic biology', *Nature*, <http://www.nature.com/nature/comics/syntheticbiologycomic/comic_text.html>; and <http://www.nature.com/nature/comics/syntheticbiologycomic/index.html>.

[84] Andersson (note 26), p. 102.

[85] E.g. Luisi, P. L. and Chiarabelli, C., *Chemical Synthetic Biology* (John Wiley & Sons: Mar. 2011).

corpse of a Native Alaskan woman buried in the permafrost for almost 80 years.[86] In 2002 *Science* published a report describing the synthesis of viable poliovirus 'from scratch' (i.e. without DNA or RNA templates).[87] Perhaps the greatest motivation for such work is to try to understand how pathogens have evolved and a general historical curiosity. It is not clear whether such work currently has clinical benefit. However, such work does add to general knowledge of the genetic and biological properties (genotype and phenotype) of ancient strains and provide context (and therefore greater understanding) to the existence and behaviour of today's 'wild type' strains and how they have evolved.

More recently, Dr Ron Fouchier of the Netherlands Erasmus Medical Centre presented findings in September 2011 that show how a modified avian influenza virus strain became readily transmissible among ferrets, the animal model he was using to study human infections, at the Fourth European Scientific Working Group on Influenza (ESWI).[88] Some biosecurity and bioterrorism commentators have expressed regret that this type of research was made permitted to proceed and argue that access to the results by the public should be restricted.[89] Such experimental work demonstrates the growing ability of scientists to re-create extinct or to create new organisms, including pathogens.

On 12 October 2011, *Nature* published a draft genome of *Yersinia pestis* (the causative agent of plague) derived from the victims of the Black Death dating from a strain associated with plague deaths in London in 1348–1350.[90] The samples were taken from the teeth of victims. They used DNA from current *Yersinia pestis* strains as a complementary template to the historical strain.[91] Analysis of the genetic structure of the strain, including its phylogeny, 'reveal no unique derived positions' as compared to those currently found in the wild. The analysis also indicates that 'factors other than microbial genetics, such as environment, vector dynamics and host susceptibility', should be the focus of analysis on epidemiology of the bacterium.[92] The researchers wished to understand why the strain that caused the Black Death was so virulent. The possible reasons include: (*a*) yet to be understood aspects of how the genes are structured in the chromosomes, (*b*) the fact that the population of 14th century Europe may have been more susceptible to the bacterium and (*c*) a combination of environmental factors, including extended warmer, wet weather and mode of living giving rise to unsanitary conditions. Finally, MacMaster University researcher Dr Hendrick Poinar noted that the ability to extract the genome would have been 'unlikely' in 2009.[93]

Professor Mitsuyoshi Ueda (Kyoto University) in collaboration with the Nara Institute of Science and Technology (NAIST) and others have developed what has been described as a

[86] Taubenberger, J. K., Reid, A. H., Lourens, R. M., Wang, R., Jin G. and Fanning, T. G., 'Characterization of the 1918 influenza virus polymerase genes', *Nature*, vol. 437 (2005), pp. 889–93.

[87] Cello, J., Paul A. V., Wimmer, E., 'Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template', *Science*, vol. 297 (2002), pp. 1016–8.

[88] <http://www.eswiconference.org/>.

[89] Greenfieldboyce, N., 'Bird flu research rattles bioterrorism field', National Public Radio, 17 Nov. 2011, <http://www.npr.org/blogs/health/2011/11/17/142453447/bird-flu-research-rattles-bioterrorism-field>; and Anonymous, 'Ophef over ontwikkeling dodelijk griepvirus' [Consternation over the development of a deadly flu virus], 25 Nov. 2011, *Radio Nederland Wereldomroep*, <http:www.rnw.nl/nederlands/bulletin/ophef-over-ontwikkeling-dodelijk-griepvirus>.

[90] Bos, K. I., et al., 'Letter, a draft genome of Yersinia pestis from victims of the Black Death', *Nature*, (12 Oct. 2011), <http://www.nature.com/nature/journal/vaop/ncurrent/full/nature10549.html>.

[91] See Schuenemann, V. J., et al, 'Targeted enrichment of ancient pathogens yielding the pPCP1 plasmid of *Yersinia pestis* from victims of the Black Death', *Proceedings of the National Academy of Sciences*, vol. 108, no. 38 (20 Sep. 2011), pp. E746–E752.

[92] Bos et al. (note 90).

[93] US Public Broadcasting Station interview of Hendrick Poinar by Ray Suarez, 13 Oct. 2011, <http://www.pbs.org/newshour/bb/health/july-dec11/blackdeath_10-13.html>.

'fundamental technology' to mass produce viral proteins through the use of a modified strain of yeast. The technique, which requires several days to employ, facilitates, in principle, the large-scale checking of substances with potential pharmaceutical benefit.[94]

Cutting edge scientific inquiry and related activity by states' national defence establishments also continue to be of particular interest from a regime compliance perspective. For example, in 2011 the UK solicited applications for a new Joint Synthetic Biology Initiative which consists of £2.4 million from the Biotechnology and Biological Sciences Research Council (BBSRC), the Defence Science and Technology Laboratory (Dstl), the Engineering and Physical Sciences Research Council (EPSRC) and the Medical Research Council (MRC).[95] The purpose of the initiative is 'to fund a cohort of preliminary, short, innovative, proof-of-concept speculative scientific investigations that seek to explore the potential applicability of synthetic biology to the UK's current and future national security and defence needs' which will be carried out 'in line with relevant international conventions'.[96] Project areas may include:

(*a*) 'research that can underpin novel sensors, detectors and diagnostic approaches, including in-field devices';
(*b*) 'development of new materials and methods for decontamination';
(*c*) 'development of new materials and methods for trauma care, including wound management and healing';
(*d*) 'smart materials and coatings, especially those that can reduce the weight of equipment'; and
(*e*) 'improvements to bioprocesses or metabolic engineering to support technology development, such as the above, with the production of biologics or small molecules'.[97]

An example of oversight by industry: the International Gene Synthesis Consortium

Of continuing interest to the parties will be how various efforts are carried out for the oversight of DNA synthesis by the industry itself. At least three major DNA synthesis standards currently exist: the International Association [of] Synthetic Biology (IASB) Code of Conduct for Gene Synthesis, the International Gene Synthesis Consortium (IGSC) Harmonized Screening Protocol and the US Department of Health and Human Services-National Institutes of Health Screening Framework Guidances. All are focused on double-stranded DNA segments 'of concern'. In November 2009 by five gene synthesis companies of the IGSC began a process of implementing a 'harmonized screening protocol for gene sequences & customer screening to promote biosecurity'.[98] The agreement covers five core components: (*a*) complete DNA sequence screening of every synthetic gene order against a pathogen database, developed by the consortium, also including screening of amino acid translated sequences (screening against US select agent lists will be included for all US domestic orders); (*b*) screening of customers for establishing identity and clearance in accordance with national guidelines; (*c*) record keeping of all orders and

[94] 'Japan: team develops technology to mass produce virus proteins using yeast', Open Source Center document JPP20110429134009. Translation of Nikkei Sangyo Shimbun (Nikkei Telecom 21: Database Version) (Tokyo)), in Japanese, 28 Apr. 2011.

[95] BBSRC, 'Call for applications—synthetic biology for new diagnostics, sensors and lightweight materials', 20 Sep. 2011, <http://www.bbsrc.ac.uk/news/research-technologies/2011/110920-pr-joint-synbio.aspx>.

[96] BBSRC (note 95).

[97] BBSRC (note 95).

[98] IGSC, <http://www.genesynthesisconsortium.org/Harmonized_Screening_Protocol.html>.

customers for up to 8 years; (*d*) order refusal at the liberty of the companies and reporting to authorities of problematic orders; and (*e*) regulatory compliance with all applicable laws and regulations governing the synthesis, possession, transport, export and import of synthesized genes and other related products.[99]

'Sequences of concern' are based on Australia Group (AG) lists (which provide whole organisms).[100] The screening attempts to look for sub-sequences that are associated with pathogenicity or which encode AG listed (or equivalent) toxins. The concept does not, at present, look for associations between DNA sequences and possible drug target receptors and the like. Rather it is agent-driven and not target-based. The typical screening length is around 200 base pairs. However, smaller units, including those imbedded into larger chunks of DNA, may be screened for.

IGSC decision making is currently based on automated screening and human review. Industry is interested to increase automated aspects given the cost and time implications of human checks. Decision-making is also time consuming as it must take into account both the sequence data and assorted data on customers, including various shipping regulatory requirements. From an industry perspective, the current operational challenges involve uncertainties over the actual understanding of what constitutes a 'sequence of concern' (e.g. Are there sequences associated with pathogenicity and thus constitutes a rational basis for assessing this?). Other operational challenges include uncertainties of how to define a 'match' between a requested sequence and a given standard, as well as the absence of a common database for making such a determination. Such a database would be essential in order to allow for full screening and decision making, partly in order to reduce the cost and time required for this activity (IGSC participants currently typically screen 2000 requests per month and fast shipments are required for optimizing vaccine production lines to match ongoing or seasonal disease outbreaks). Sequence data is becoming increasingly relevant as the capacity for synthesis increases.

It should also be noted that it is possible for actors who require DNA sequences (regardless of whether double- or single-stranded) to bypass such voluntary systems, including through the use of shorter DNA fragments (i.e. oligonucleotides, typically 20–40 base pairs), the use of synthesizers and extraction directly from nature. However, the use of pre-ordered DNA sequences is convenient and many in the research community and in industry continue to 'out source' their DNA synthesis.

In terms of transparency and possible investigations of misuse, DNA sequences may be 'tagged' in order to indicate their origin. It is also straightforward to differentiate between a system developed on the basis of synthesized DNA sequences and those based on 'wild forms' (i.e. in nature).

The global turnover of DNA synthesis has risen to around $(US)200 million, a small fraction of the overall synthetic biology market. The DNA synthesis companies are mostly located in China, Europe and the US. The oligonucleotide market, however, is much larger and more widely dispersed than the DNA synthesis market (with many regional/local suppliers ensuring fast supply where needed; also oligonucleotide screening poses conceptual problems of association between sequences and pathogenicity, given the small size of the molecules). Of some concern is how such guidelines can deal with 'split orders'

[99] International Gene Synthesis Consortium (IGSC), Harmonized Screening Protocol, undated, <www.genesynthesisconsortium.org/.../IGSC%20Harmonized%20Screening%20Protocol.pdf>.

[100] The summary of the implementation of the guidelines is based on discussions that occurred during the meeting convened by SIPRI: *Addressing Future Challenges to the Biological and Toxin Weapons Convention in Connection with Scientific and Technological Developments*; 5–6 Mar. 2011; Stockholm.

whereby an actor may attempt to circumvent controls by dividing DNA segment orders so that they do not raise 'red flags' in the system.[101]

With regard to directions that the Seventh Review Conference could give or reinforce, DNA synthesis is an example for how controls and oversight mechanisms of governments can and should be combined with internal governance mechanisms of the industry. In a field as dynamic as this (and where the industry needs to be able to rely on fast screening and decision making processes to remain competitive), longer-standing government control approaches (as, for example, used in traditional transfer controls) may simply be to cumbersome and time consuming. Despite their limitations, control measures implemented by companies themselves will be increasingly important, as will cooperative relations between companies and governmental control authorities that enable either of them to flag problems and attempt to resolve specific issues. It should also be noted that the 'catch-all' mechanism in transfer controls would still function as intended, provided the informal mechanisms between industry and state licensing authorities operate well.

If that is accepted, then what is equally important is to harmonize: the approaches to screening of customers and orders, the databases used in these processes, and decision making as to whether or not to accept an order in the first place. Governments can play a critical role in helping to create—in collaboration with industry—such standards at the international level.

Implications for the BTWC

Synthetic biology (including synthetic genomics) is likely to remain a field of research and industrial activity that require both monitoring and assessment from a BTWC compliance perspective. Efforts to provide effective and adequate governance through a combination of regulatory and self-regulatory measures should continue. The science and industry communities should be expected to show considerable interest in developing effective public education and awareness raising strategies.

This field is prone to misrepresentation and misperceptions regarding potential risks to the public and the environment. These, as well as overstated risks associated with a possible misuse of synthetic biology for hostile and weapon purposes, could hinder progress in this important field of research and slow the evolution of cooperative research and industrial activity. Many future beneficial applications of synthetic biology will require a favourable, yet well-governed, environment.

Simultaneously, synthetic biology is an activity at the intersection of several S&T disciplines. Specific outcomes and discoveries are inherently uncertain. Systematic monitoring of advances and assessment of their implications (not with regard to compliance, but of the emergence of new potential misuses) will therefore be necessary for future S&T-related mechanisms under the BTWC.

III. Systems biology and bio-informatics

Systems biology may be defined as the modelling and simulation of sub-cellular, cellular and macro-scale phenomena. The aim of such models is encoding and testing hypotheses about mechanisms underlying the functioning of cells. Molecular networks are a typical example where the behaviour of cells is expressed in terms of quantitative changes in the

[101] Schmidt, M. and Giersch, 'DNA synthesis and security', p. 12 in Ed. Marissa J. Campbell, *DNA Microarrays and Synthetic DNA* (Nova Science Publishers: 2011).

levels of transcripts and gene products. Bioinformatics provide essential complementary tools, including procedures for pattern recognition, machine learning, statistical modelling (testing for differences, searching for associations and correlations) and secondary information streams extracted from databases.[102] The purpose of this kind of research is to understand how biological systems actually function at the cellular level. This can then serve as a basis for the design of new drug candidates or, of course, candidates for biochemical warfare agents.

Such developments have been made possible by an explosion in computational power and the ever-expanding use of the Internet for the sharing of experimental data, methods (e.g. open software) and computation power (e.g. cloud computing). Equally important has been the evolution of such techniques as functional imaging of target areas of new drug candidates, or areas associated with physiological functions.

This research remains data heavy and 'light' on theory. Progress is driven more by the ability to store, organize, share and process vast amounts of data, rather than by an ability to connect the data in a useful conceptual manner that would generate new insight and knowledge. This is partly a reflection of the quality of the available data (e.g. with a lack of standards in protocols used in past research). It also reflects a general lack of conceptualization and organization theory necessary to extract knowledge from the data regarding the function of complex biological systems. Nevertheless, the evolution of systems biology and bio-informatics will foster change in the life sciences from a primarily descriptive discipline to an increasingly predictive one. As this occurs, the potential inherent in biology for beneficial (and hostile) applications is certain to increase exponentially.

Implications for the BTWC

From a regulatory point-of-view, advances in systems biology and bio-informatics deserve continued monitoring and evaluation.

Existing trends in the field will yield new understandings and knowledge that will result in previously unsuspected applications for peaceful purposes. Perhaps more significantly, as previously mentioned, such research 'piggy-backs' on the evolution of the Internet, including the creation of shared data storage, open scientific software applications and distributed, decentralized computational capacity. This environment inherently promotes collaboration across national and regional boundaries. It is less dependent on 'heavy, up-front' investment. And it encourages broad national and international participation in research projects. These developments are positive from the perspective of effective implementation of Article X of the BTWC on the fostering of economic and technological development.

It is important for the parties to the BTWC to recognize the implications for any paradigm shift in the life sciences emanating from advances in this field for the implementation of Article I of the convention. Should such a shift occur, risk assessments concerning BW threats might have to be reconsidered and revised.

[102] Wolkenhauer, O., et al., 'SysBioMed Report: Advancing systems biology for medical applications', *IET Systems Biology*, vol. 3, no. 3 (2009), pp. 131–36.

IV. Brain research

The British Royal Society has undertaken a series of studies as part of its 'Brain Waves Project'.[103] Current and future modules will cover conflict, security and legal issues.[104] A growing ability to determine and influence brain function opens a potential range of non-traditional state BW programme activity. Professor Steven Rose has identified five principal conflict/control dichotomies: (*a*) lethal/non-lethal agents, (*b*) military/civilian purposes, (*c*) enhancing/degrading effects (*d*) physical/biochemical effect and (*e*) central nervous system/peripheral nervous system. He has also characterized potential novel agents according to (*a*) non-cholinergic or opiod agonists (receptor or reuptake inhibitors), (*b*) 'memory erasers', (*c*) 'trust inducers' (e.g. oxytocin), (*d*) 'mood modifiers', and (*e*) agents derived from non-traditional drugs (e.g. peptides).[105]

New instrumental and investigative techniques, including brain imaging techniques and advances in neuropharmacological agents, have led to insights that could result in more selectively acting agents that interfere with cognition, mood, performance and other human brain functions.[106] In the context of evolving military requirements (particularly 'military operations other than war' such as policing functions, peace keeping missions, as well as traditional covert operations) such advances may create demand for 'non-lethal' biochemical agents.[107] There are scientific reasons to question whether such agents can in fact be developed to be effective, reliable and safe.[108] However, advances in the neurosciences may still result in developments that risk undermining the international legal prohibitions against chemical and biological warfare.[109]

The parties to the BTWC should further consider whether and how to implement S&T mechanisms in a manner that takes such dichotomies and potential novel agents into account. Such awareness by the policy community of the possible longer-term implications for the norms banning chemical and biological warfare serves to support the regime's institutional capacity to reach common understanding on the legality of such programmes in future.

V. Targeted drug delivery

Targeted drug delivery has been a goal of pharmaceutical research for decades.[110] The objective is to selectively deliver a drug to the target organ or tissue and thereby decrease

[103] *Brain Waves Module 1: Neurosciences, Society and Policy* (The Royal Society: London, Jan. 2011); and *Brain Waves Module 2: Neurosciences: Implications for Education and Lifelong Learning* (The Royal Society: London, Feb. 2011).

[104] See UK Royal Society, Policy Projects *Brain Waves*, <http://royalsociety.org/brainwaves/>.

[105] Rose, S., 'Future challenges to the BTWC: neuroscience', SIPRI Workshop on the BWC Review Conference, 5–6 Mar. 2011.

[106] For general background on the current application of neuroinformatics, convergent technologies and brain imaging for medical treatment, see Baycrest, Research Annual Report, 'A guide to brain imaging technologies', <http://research.baycrest.org/brain-imaging-technologies-guide>. Baycrest is a Canadian health care provider organization based in Ontario.

[107] Tucker (note 77).

[108] Klotz, L., Furmanski, M. and Wheelis, M., *Beware the Siren's Song: Why 'Non-lethal' Incapacitating Agents are Lethal* (FAS: Washington, DC, 2003), <http:www.fas.org/bwc/papers/sirens_song.pdf>.

[109] International Committee of the Red Cross (ICRC), *Incapacitating Chemical Agents: Implications for International Law* (ICRC: Geneva, Oct. 2010).

[110] E.g. Delehanty, J. B., et al., 'Peptides for specific intracellular delivery and targeting of nanoparticiles: implications for developing nanoparticle-mediated drug delivery', *Therapeutic Delivery*, vol. 1, no. 3 (2010), pp. 411–433.

the dose necessary to cause a therapeutic effect. Doing so allows medical practitioners to reduce the toxic (acute and chronic) side effects during drug treatment. To this end, it is important to achieve a better understanding of the functioning and structure of the target structures (at the receptor, cellular and tissue levels), as well as of the biological barriers that must be crossed (e.g. the blood–brain barrier). Advances in drug delivery are making use of new drug formulations and particle engineering techniques, including microfluid technology, nanotechnology, microencapsulation, viral vector technology and the use of immunotoxins and fusion proteins as vectors.[111]

Much attention has recently been devoted to advances in nanotechnology which can be defined as the development and use of applied S&T at macromolecular ranges of approximately 1–100 nanometres (one nanometre equals one billionth of a metre).[112] The fabrication of devices on this scale is a multidisciplinary undertaking that encompasses the fields of biology, chemistry, materials sciences and physics. Bio-nanotechnology offers the ability to insert non-soluble substances into various aqueous environments. Thus, 'dry' inorganic nanomaterials can be developed to function or react with 'wet' biological systems. In principle, this allows for the development of novel drug delivery systems. For example, Sangeeta Bhatia and her colleagues at the Massachusetts Institute of Technology (MIT) published findings in 2011 that uses the body's natural signalling mechanism for blood clotting to attract drug delivery particles to a tumour site.[113] Bio-nanosensors are also being developed to produce digital electronic signals to indicate various biological processes within an organism (e.g. to indicate levels of glucose in the blood of those suffering from diabetes).

Anti-cancer conjugates have also long been a topic for targeted drug delivery.

VI. Bioforensics

Bioforensics refers to a variety of methods and concepts used in investigations of biological incidents, including disease outbreaks. This is an area of research that has seen considerable progress in recent years that was partly driven by the 2001 mailing of letters filled with *Bacillus anthracis* spores to politicians and members of the media in the USA.[114] In the case of a deliberate release of a biological agent, bioforensic methods may provide evidence that can be used for attribution purposes. An early example of this was gene sequencing. However, additional methods are also being employed. The time and cost needed to sequence genes has dropped dramatically, and the target of sequencing an entire human genome at a price of US$1000 is now feasible. In addition, the genomes of some

[111] Nixdorff, K., 'Advances in targeted delivery technology', Report of the research group on the life science revolution and future biochemical control', (Aug. 2008).

[112] See 'Issues in nanotechnology', *Science*, vol. 290, no. 5496 (24 Nov. 2000).

[113] Von Maltzah, G. et al., 'Nanoparticles that communicate *in vivo* to amplify tumour targeting', *Nature Materials*, vol. 10 (2011), pp. 545–552. See also <http://www.nature.com/news/2011/110619/full/news.2011.374.html>.

[114] For recent developments concerning the US National Academies of Science evaluation of the validity of the science employed by the Department of Justice, see Committee on Review of the Scientific Approaches Used During the FBI's Investigation of the 2001 Bacillus anthracis Mailings, Board on Life Sciences (Division on Earth and Life Studies), and Committee on Science, Technology, and Law Policy and Global Affairs Division, *Review of the Scientific Approaches Used During the FBI's Investigation of the 2001 Anthrax Letters* (National Academies Press: Washington, DC, 2011); FBI, 'Amerithrax or anthrax investigation', <http:www.fbi.gov/about-us/history/famous-cases/anthrax-amerithrax>; Department of Justice, 'Amerithrax documents', <http://www.justice.gov/amerithrax/>; and Public Broadcasting Service, Frontline, 'The Anthrax Files', 21 Oct. 2001, <http://www.pbs.org/wgbh/pages/frontline/anthrax-files>.

6500 organisms have been sequenced, creating a huge global depository of genomic data for analysis and research.

Epigenetic refers to inheritable DNA traits of living cells that remain stable following cell division (e.g. mRNA). This is key to understanding the genetic heritage of microorganisms which, in turn, can also serve as markers for identification of the origin of a given strain and is therefore an important part of microbial forensics.[115] Knowledge of epigenetic processes, such as the regulation of histone modification, could also be misused.

Implications for the BTWC

From a BTWC perspective, these advances contribute to the methodology and tools available to discriminate between natural outbreaks and disease caused by deliberate releases of biological or toxin agents. These can also be applied in a manner relevant for BTWC compliance assessments in that they allow for attribution of certain activities associated with the development or preparation of BW agents.

[115] Budowle, B., et al., *Microbial Forensics*, second edn. (Academic Press: Burlington, MA, 2011).

4. The interface between S&T developments and the BTWC: recommendations

There are a variety of BTWC implementation issues that may be said to be at the interface of S&T developments and which have policy and technical implications for the future of the regime.

These include how to deal with compliance (e.g. scope of prohibition, legality of certain biodefence activities). Regulatory requirements are also areas where self regulation is necessary. Risk assessment management, including horizon product screening and in-depth toxicological and pharmacological property studies are also needed.

States should further consider the exchange of information and other transparency measures such topics as (*a*) whether they possess mechanisms in place to review the legality of research and development activity (civilian and military) under international law (including the BTWC), (*b*) the results of such reviews along with the main technical and legal points which served as the focus of the review, (*c*) the existence and potential relevance other regulatory and oversight mechanisms (including those concerning 'whistle blowers').[116]

Article X on economic development and cooperation may also be viewed as an S&T (including through capacity-building) basket of issues. This has two aspects: on the one hand, advances in S&T occur in an international context and the BTWC encourages international cooperation among its Member States in S&T. To avoid hampering the development of the States Parties, regulatory steps taken to implement BTWC requirements must be such that they do not conflict with these development goals. The Seventh Review Conference presents another opportunity to exchange information and experience among the Member States about effective ways of implementing the BTWC at the national level, and doing so without adverse effects on international cooperation (including in relevant areas of S&T).

At the same time, the advances in S&T and the evolving nature of scientific collaboration using modern means of communications *themselves* (e.g. over the Internet) create new opportunities for international cooperation and the strengthening of expertise. It will be important that the Member States understand and fully appreciate this so as to be able to undertake specific steps to further enhance international cooperation, and also to avoid measures that would undermine this evolving collaborative framework.

The Review Conference could perhaps agree an intersessional process in which, inter alia, the States Parties table specific proposals for how to fully and effectively implement Article X, such as through joint-training, research and publication. An effort could also be made to link the results of S&T evaluations to the provisions of Article X.

An example that may be worthwhile scrutinizing for its relevance to the BTWC processes is the workshop undertaken by the OPCW in 2010 on future opportunities to implement Article XI of the CWC (which essentially is the equivalent to Article X of the

[116] For one discussion on the importance of such transparency, see Roffey, R., Hart, J. and Kuhlau, F., 'Crucial guidance: a code of conduct for biodefense scientists', *Arms Control Today*, vol. 36, no. 7 (Sep. 2006), p. 20. Parties to the BTWC could also exchange information on their respective 'confidentiality policy and possible "whistle blowing" regulations and procedures at facilities engaged in classified biological-related work'. Hart, J., 'Improving confidence-building measures under the Biological and Toxin Weapons Convention (discussion paper)', p. 4. Paper presented at the 29th Workshop of the Pugwash Study Group on the Implementation of the Chemical and Biological Weapons Conventions: *Moving Towards the Seventh BWC Review Conference*; 29–30 Nov. 2008; Geneva, Switzerland.

BTWC).[117] This workshop was an interactive 'brain-storming' exercise that brought together representatives of CWC states parties, academia, industry, interested NGOs and individual experts knowledgeable in the field, in an effort to develop a common understanding of the objectives of that provision of the CWC and, most importantly, to develop and examine practical proposals for the implementation of measures that would further enhance international cooperation. A participant from Azerbaijan, for example, suggested the creation of 'scientific communities websites' and the formation of internet-based cooperation and information exchange for scientific and experiment design activity in order to promote scientific cooperation.[118]

The context of the BTWC is, of course, quite different, having no international agency or treaty organization specifically tasked to implement programmes in the field of international cooperation in areas relevant to the Convention. However, there are indeed international actors who implement programmes that are relevant to this objective, and a similar workshop approach could perhaps bring these actors and the Member States closer together. The actors could be selected partly on the basis of the following criteria: (*a*) area of S&T and relevant enabling technology, (*b*) base research, (*c*) development, application and scale-up of relevant S&T and associated enabling technologies and (*d*) due regard to equitable geographic distribution. Such a workshop could also help to define better what role, if any, the ISU could play in the future to promote the implementation of Article X. The Seventh Review Conference could call for such an exercise, involving a wide range of stakeholders (including member states and the ISU) so as to develop practical suggestions for what can be done to foster Article X implementation in a practical manner.

I. Intersessional process

The principal question with respect to a possible further intersessional process after the Seventh Review Conference is to agree what topics BTWC parties should consider, and how these considerations can be transferred into actions or decisions.[119] Currently, it would appear that three baskets of issues could, in principle, be agreed as suitable for an intersessional process:

(*a*) effective implementation,
(*b*) universality and
(*c*) S&T.

Effective implementation allows the parties to consult each other on how best to maintain and strengthen the capacity of the regime in order to understand compliance issues arising from, for example, the annual data exchanges meant to act as CBMs. Such consultation

[117] 'Workshop on Article XI of the CWC at OPCW headquarters', OPCW press release, 26 Nov. 2010, <http://www.opcw.org/news/browse/5/article/workshop-on-article-xi-of-the-cwc-at-opcw-headquarters/>.

[118] Kalbalieyeva, E., 'Promoting networking and exchange among scientific communities, academic institutions, chemical-industry associations, NGOs, and regional and international institutions', p. 4, (note 117).

[119] In June 2011 Richard Lennane suggested an intersessional process structure based on three working groups: (a) WG1: Implementation and compliance, (b) WG2: Science and outreach and (c) WG3: Cooperation, assistance and capacity-building. The five-day Meeting of Experts would devote one day to each of the working groups, while the fourth day would be on a 'special topic' that varies each year. The fifth day of the expert working group would be devoted to 'other matters' and the drafting of the final expert group report. Lennane, R., 'Structure of the Intersessional Process', slides 6–7. Presented at *Outlook and Perspectives for the BTWC Seventh Review Conference*, 9-10 June 2011, Berlin. It is reasonable to suppose that some informal consultation took place on this structure, prior to its being presented, or that the proposal was informed by interactions with a number of the Member State representatives and reflects what might have been seen as a possible consensus approach.

would also allow a continuation of discussions regarding national implementation measures (legislation, regulations, transfer controls and other administrative measures), as well as other governance measures (outreach and cooperation with industry, involvement of science organizations, other NGOs and civil society). It may open opportunities to further develop technical assistance concepts under the BTWC to strengthen implementation at national, as well as regional levels.

Insights into operational challenges may, perhaps, be found in the work of other multilateral activity such as the UN Counter-Terrorism Committee, the Al-Qaida and Taliban Sanctions Committee, the 1540 Committee Concerning the Non-proliferation of Weapons of Mass Destruction, and the UN Global Counter-Terrorism Strategy. A characteristic dichotomy of such activity is often one between legal or policy commitments made at the higher political level versus the technical expertise and capacity required to implement such commitments. It is not unusual to encounter a great gap between the two. Discovering the nature and reasons for such gaps can therefore be a highly useful activity. A related consideration is that it is often easier for states to engage in narrowly focused technical activity (e.g. one that involves consultation or cooperation) than activity that includes mainly political and policy interaction.

Universality is a topic that requires engagement with the non-members and is, therefore, somewhat less amenable to being fully addressed through a process of annual meetings. The ability of the parties to promote universality through an intersessional process may therefore be limited if this process consists solely of annual Meetings of Experts and States Parties. Such meetings could nevertheless be used for consultations among BTWC parties to review any progress with regard to universality, and to discuss options for how to encourage non-parties to join. The Review Conference could task the ISU to prepare background material analysing possible reasons for their absence, for example, based on compilations of responses by the non-parties to inquiries made by the ISU on behalf of the BTWC parties collectively or individually.

But more important would be the activity of Member States and the ISU between meetings of the intersessional process. Opportunities for specific measures that they could undertake could emerge from contacts outside the BTWC context (e.g. in the context of activities of the UN, the 1540 Committee, or regional activities), or those that could be pursued by Member States and/or the ISU on a bilateral or regional basis involving non-members.

The Seventh Review Conference could also decide to invite non-members to intersessional process meetings. The structure of how they would interact with other participants and what (if any) input would be requested of them would have to be given careful consideration. If, for example, the non-member participants were asked to make presentations on their views concerning the international prohibition against biological warfare, this could present a risk that the topics discussed at the meetings could expand and become overly diffuse and fraught with political tension. Such a meeting might also replicate discussions in other forums on attempting to achieve a Middle East free from WMD. Alternatively, the non-member states could be ‘button-holed’ at the margins, assuming they agreed to attend. Thus it is possible that an intersessional process could be structured in a manner that effectively serves as a ‘track-2’ framework in which to engage the non-Member States. Such engagement could include consideration of:

(*a*) the extent to which a non-Member feels it is useful to indicate the importance it attaches to the object and purpose of the Convention,
(*b*) the nature and scope of a possible CBM data submission,

(*c*) the degree to which it wishes to engage in consultation, clarification and fact-finding on compliance-related matters (either to receive or to request), or
(*d*) the nature and type of interest in national, regional multilateral capacity-building.

A complementary process could consist of regional meetings with the participation of States Parties and non-parties in order to create a degree of 'peer pressure'. Such a process can be useful (as experience from both BTWC and CWC universality initiatives have shown) in order to raise awareness, promote political support for the BTWC, facilitate a better understanding of the requirements for a given state to join the regime and (where necessary) identify means of external support (e.g., practical support with necessary legislation, education and outreach to stakeholders, political advocacy with regard to policy makers and parliamentarians, 'twinning' with countries who can assist the prospective member state).

Advances in *S&T* affect the implementation of the BTWC at several levels. With regard to the prohibitions, new and evolving risks need to be addressed—both with respect to the transparency of state programmes in the area of biodefence and relevant activities associated with non-state actors. S&T advances have also had an impact on the prospects for BTWC verification. All require further and periodic evaluation in the BTWC context. The exact scope and phrasing would have to agreed partly on the basis of drafts tabled by the parties and follow-up consultation before and during the review conference. The Review Conference could consider agreeing language (*a*) to identify and address the purpose of S&T reviews for the regime, (*b*) to consider further the criteria for 'success' of any such review and (*c*) to consider mechanisms to achieve identified S&T-related objectives. More specifically, the parties could consider various S&T evaluation methodologies used outside the biological arms control context, such as for broader national security, economic cooperation and development, patent guidelines and practice, assessment of scientific training and research and select case studies.

II. Other considerations

There may be some flexibility among the BTWC parties to explore new ideas for enhancing and strengthening measures to demonstrate compliance to the regime in a manner that takes due regard to the principle of equal obligations and responsibilities among the members that is inherent to any multilateral arms control and disarmament regime.

There is a continuing need for constructive engagement among the BTWC States Parties for structural stability within the regime; for further exchange of views; and relevant, agreed activity to develop a better understanding of the relation between CBM submissions and compliance. A need also exists for more effective mechanisms to remain aware of S&T developments in general and how they may affect the implementation of the BTWC prohibitions in particular.

Consideration of what constitutes a biological weapon is heavily influenced by the activity of traditional state military programmes. This is so partly because reference to historical large-scale state programmes are less susceptible to definitional or legal dispute. Also those who refer to historical state programmes are less likely to be accused of publicizing or exaggerating future biological warfare threats. Today there is much debate and confusion among states, analysts and interested observers over whether activities utilizing recent S&T developments for non-traditional purposes such as counter-terrorism

operations are permitted under the BTWC. Specific S&T developments should therefore be considered in terms of possible non-compliance in a manner that informs and supports the legal norm, while avoiding to advertise unorthodox methods for conducting biological warfare.

The parties should therefore further consider what, if any, activity related to applied S&T developments they believe to be indicative of a possible violation to the BTWC. In parallel, they should take all necessary steps to ensure that they understand the principal threats associated with S&T developments to the object and purpose of the Convention.

The Seventh Review Conference should not focus on the content of S&T per se, but rather consult and agree on the most effective mechanisms to bridge S&T with political and legal requirements associated with the full and effective implementation of the BTWC.

5. Conclusions

The four overarching questions posed by this study were:

1. What is an 'activity of concern' in the new S&T environment (and can one even usefully apply a concept of such 'activity of concern' in the dual-use context of the life sciences)?
2. What is the appropriate policy response with respect to both general S&T trends and developments and possible future specific activities that may require regulation and other governance responses? and
3. What is the expected operating environment of the BTWC over the coming 10–20 years?
4. Based on discusssions and consultations in 2011, it seems likely that an intersessional process will be agreed and that S&T will be reflected in the work programme. Whether and how should this topic be incorporated?

Many S&T advances have increased the potential (in the form of knowledge, material and technologies) that could be misused if the life sciences were to be applied for hostile purposes. Yet, on their own, they do not lead to the emergence of new biological warfare options. What matters is rather the context in which these life sciences activities is carried out. For example, threat assessment and biodefence programmes (depending on how they are structured and implemented) can, if carried out with a lack of sufficient transparency, raise concerns among other states or actors regarding their legitimacy or intent. This, in turn, can have destabilizing effects on the BTWC regime. However, it is not the nature of the research itself that should be the focus of clarification and evaluation by the parties. While science monitoring can assist in the identification of new discoveries or research activity, what is most important is an in-depth evaluation of their implications for the regime. In particular, the parties should understand whether these new scientific activities and discoveries lead to paradigm shifts and, therefore, call for new approaches and responses in the context of biological arms control. This can be done by the parties (both individually and collectively) in the context of possible future intersessional processes. A mechanism for evaluation and review is more important for the stability and sustainability of the norm against biological warfare. Such a mechanism should also become more systematic and participatory in nature.

With regard to policy responses to S&T trends, the very nature of the life sciences calls for a combination of top-down regulation based on the principles and norms of the BTWC, and a bottom-up approach of self-regulation and voluntary measures to increase transparency and to strengthen responsible conduct in research and life sciences application. Both avenues are important, as is the interaction between governments and regulators one the one hand and science and industry communities on the other hand. Scientists need to have the freedom to carry out research and publish new discoveries and methods. Industry requires a predictable and fair environment in which to conduct business. Governments require the necessary tools to ensure that all relevant actors in the life sciences remain compliant with BTWC norms and the various relevant mechanisms in place to resolve compliance issues vis-à-vis other parties to the convention. The entire enterprise is both multidisciplinary and driven by overlapping interests and responsibilities (of governments, private enterprise and the life science community at large). Effective international biological arms control calls for a combination of a traditional regulatory

approach and the more fluid networking solutions that bring together a wide range of actors.

As to the future operating environment of the convention in the coming years, attempting predictions is problematic as they are generally incorrect. Rather, the focus should be on major trends and 'drivers', many or most of which can be readily identified now. Several such factors are worth noting. As the cost of key enabling technologies (e.g. computing, synthesis, screening) drops and the international capacity to utilize them increases, the traditional distinctions between 'donors' and 'recipients' of technology transfer will become increasingly irrelevant. In this regard, the world is already living in 'post-proliferation' environment which is characterized less by the proliferation of weapons, but rather by an increasing accessibility to and capacity for work in life sciences and related technology.

The Review Conference could consider ways to provide a degree of structure or direction to future S&T activity. In the final document, the conference might consider including 'markers' of areas of particular relevance such as enabling technologies. Some 'markers' could be linked to inter alia the full implementation of Articles I and X.

Irrespective of any specific insight into the future of the understanding of the life processes, the ability of scientists to *manipulate* (rather than *kill*) humans and other organisms will increase. The future of biological and chemical warfare (if there is one) will entail the creation of agents that *specifically* interfere with the life processes. Possibilities for misapplication include the capacity of soldiers to fight, the ability of the human body to resist infection and disease, the safety of the food chain, and the economic well-being of the agriculture.

Nevertheless, the prospects to use the life sciences for beneficial purposes is enormous. Whatever regulatory framework that is further developed and implemented to manage this emerging field (including the expected qualitative—and hence revolutionary—leaps in understanding of the functions of life) it is vital to ensure that progress in scientific discovery is not hindered and that effective mechanisms exist to prevent its perversion for CBW purposes. This entails, among other things, a new approach to define the relationship between the scope of the BTWC's prohibitions and its aspiration under Article X to promote international cooperation in the field of peaceful applications of biology.

With regard to compliance assessments, any system of analysis pre-supposes the existence of patterns, order or relationships where none may exist. Government officials and analysts may also assume that objective facts can be discovered and understood. Alternatively one can view efforts at obtaining a greater understanding as an iterative process towards progressively better understanding. In philosophy and elsewhere, observers sometimes note the risks posed by 'determined' or 'over-determined' outcomes.[120] Two questions regarding the nature of human understanding that have relevance for arms control compliance assessments is: (*a*) whether objective truth exists and is discoverable, and (*b*) whether human perception is mediated by a first observer and second person recipient. In other words, a first and second order mediation of observed events exists. The first view holds that objective truth exists and is discoverable and emphasizes explanation. The second view (regarding mediation of human perception) stresses an inherent subjective quality to understanding. A further complication is that states will always have a tendency to seek politically preferred outcomes or passively fail to act in cases where politically painful outcomes are involved.

[120] Treverton, G. F., *Intelligence for an Age of Terror* (Cambridge University Press: Cambridge, NY, 2009).

Finally, the most important objective of the regime (and the Seventh Review Conference) is to maintain and strengthen the international norm against biological warfare. Another fundamental objective is to maintain and strengthen a framework through which the parties can inform themselves of political and technical developments that could affect the full implementation of the convention, including those involving economic cooperation and assistance and S&T, and develop agreed approaches to governance in order to address identified challenges.

Annex A. Policy options

The following are options for practical steps that could the Seventh Review Conference might consider, and include in its final documents. Elements of such an intersessional process include:

(*a*) agreeing several 1-week expert meetings that lead into subsequent discussions and, if necessary, decisions at the Meetings of States Parties;
(*b*) distinguishing formal meetings from exploratory talks (or exploratory consultations);
(*c*) developing concrete measures or decisions to support the 2012 meeting on a WMD free zone in the Middle East. This could include text on the desirability of including biological and/or chemical weapon-related topics in the agenda. Some thought would have to be given to the mechanism for helping to ensure that this could, in fact, be carried out. For example, a facilitator could be designated or this activity could be placed under the direction of the chair of the respective third intersessional meetings. Also, the ISU could be given authority to compile, based on member states input, the background documentation referred to in the decision on the 2012 meeting taken by the NPR Review Conference on 2010; and
(*d*) a work programme with relevant stakeholders (i.e. industry, research communities, teaching and educational communities, NGOs and civil society at large).

The Review Conference may decide to retain, modify or replace the standard phrasing from the first and second intersessional processes. In short, should a third intersessional process task the annual meetings of experts and states parties to 'discuss, and promote common understanding and effective action' on the agreed topics?

I. Compliance

Options for activities relevant to resolution of compliance issues may be developed in terms of illustrative intersessional discussion topics (see tables A.1 and A.2).

Table A.1. Illustrative topics for the effective implementation of Article I

- Mechanisms to discuss methodologies and share results of work on detection paradigms and systems for improved, emerging and novel biological threats,[121]
- Clarify (and procedurally streamline) the relationship between the UN Secretary-General's mechanism to investigate alleged use of chemical and biological weapons and the BTWC Article VI clarification procedures,
- Current best practices for the handling and analysis of mixtures of chemical, biological and radiological agents (so-called 'mixed samples').[122]

Source: Author compilation.

[121] *High-Priority Technology Needs*, *version 3.0* (US Department of Homeland Security, Science and Technology Directorate: May 2009), p. 15.

[122] E.g. dichloromethane is a common solvent for the extraction of standard chemical warfare agents from environmental samples. However, it also can promote bacterial growth and is therefore perhaps not suited for sample extraction for some types of potential biological warfare agents. It should also be noted that this topic would promote a better understanding of the interface between the biological and chemical weapons arms control regimes.

Table A.2. Elements of CBM template to allow for submissions of S&T review

Principles/objectives ▪ Areas of S&T subject to the review ▪ Methodology (e.g., expert study, technical workshop, peer reviewed paper, etc.; institutions/key experts involved) ▪ Main sources used (e.g., reference to key publications, patents, etc.) ▪ Impact on the BTWC implementation process
Measures proposed to be taken as a result of the assessment ▪ References to any published documents that resulted from the review ▪ Criteria having potential applicability to S&T oversight mechanisms

Source: Author compilation.

II. Science and technology

Text regarding a third intersessional process that deals with S&T could be modelled on the phrasing of the first two intersessional processes. Possible topics include:

(*a*) S&T oversight and review methodologies and their potential relevance of transparency and accountability in the context of the Convention;
(*b*) Developments in the life sciences relevant to maintaining the effectiveness of the international prohibition against biological warfare (Article I) and their potential effect and relevance on international cooperation and development (Article X);
(*c*) Informal discussions between BTWC and CWC regime experts (e.g. with involvement of the OPCW and its Scientific Advisory Board) on developments in chemistry relevant to maintaining the effectiveness of the international prohibition against biological warfare (Article I) and their potential effect and relevance on international cooperation and development (Article X);[123]
(*d*) Developments in enabling technologies including information technology (e.g. data mining)[124] relevant to maintaining the effectiveness of the international prohibition against biological warfare (Article I) and their potential effect and relevance on international cooperation and development (Article X); or
(*e*) Possible conclusions and recommendations for the consideration of the Eighth Review Conference on appropriate and effective S&T oversight and review methodologies for enhancing transparency and accountability in the context of the Convention.

III. Article X

The parties could be invited to provide to the ISU for posting on the UN website specific requests for activities potentially falling under the provisions of Article X for cooperation

[123] It should be noted that the SAB currently has a working group on convergence of chemistry and the life sciences. States and other interested parties should examine the group's methodology and findings in 2012 for their possible relevance to biological arms control.

[124] Data mining, Knowledge Discovery in Databases (KDD) or Knowledge-Discovery and Data Mining refers to automated searches of large volumes of data for patterns. Of possible relevance to Article I is the data mining that is carried out using various network analysis tools and whose key objective is to link data patterns to criminal or terrorist activity. In this context, two main objectives are (*a*) 'how to align the data models of multiple data sets', and (*b*) 'how to build advanced algorithms that can work across multiple data sets'. Office of the Director of National Intelligence 2009 Data Mining Report for the Period of February 1, 2009 through December 31, 2009', p. 3.

and assistance. Other parties may offer (singly or cooperatively) proposals for implementing such requests.

The conference could underline the importance the parties attach to providing tailored and sustainable implementation support for the full implementation of the convention. To this end, the conference could agree that:

(*a*) the ISU could collect and collate from the parties during the intersessional process requests for cooperation and assistance under Article X;
(*b*) parties (individually or collectively) are encouraged to propose measures and activities to implement these requests;
(*c*) the ISU could collate requests and responses and any results of such activities to the Eighth Conference of the States Parties; or
(*d*) the parties involved in such activity are encouraged to share 'lessons learned' and proposals for the improvement of such activity including by decisions taken by the Eighth Conference of the States Parties'.

The conference could agree guidelines to help inform the submission of requests for cooperation and assistance under Article X. Such guidelines could include:

(*a*) overview papers
(*b*) selected S&T areas, and
(*c*) criteria and principles for success.

Table A.3. Illustrative topics for the effective implementation of Article X

▪ Overview papers (political, legal, technical, scientific)
▪ Operational, time-limited proposals/requests
▪ Operational, time-limited proposals/offers

Source: Author compilation.

Table A.4. Illustrative topics for annual Meetings of States Parties

▪ Regulatory frameworks that involve the implementation of S&T review methodologies,
▪ The manner in which 'meta-experts' are formed and how authoritative and useful are their findings (in general terms and with practical case studies),[125]
▪ Chemistry developments that are relevant to the effective implementation of Articles I and X (e.g. prediction of human physiological effects of pharmaceuticals, best practices from cooperative mechanisms/models for acquiring patent rights for base and applied research in the life sciences)

Source: Author compilation.

IV. Other

The Seventh Review Conference could agree a process in which the parties, the research community, industry, academics, NGOs and civil society are able to exchange views and information on the various methodologies and purposes for which S&T reviews have been undertaken.

[125] Difficulties associated with the formation of such groups include: the appointment process, and the validity and weight that should be attached to minority or dissenting views.

The Review Conference could task the ISU to prepare background material analysing possible reasons for the absence of States not part from the BTWC. For example, this could be based on compilations of responses by the non-parties to inquiries made by the ISU on behalf of or by the BTWC parties (individually or collectively).

Factors currently available to facilitate better cooperation in the life sciences among researchers and regulators. The ISU could facilitate a series of seminars on a limited number of practical areas with a view towards identifying opportunities to improve S&T cooperation among the parties.

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