Trends in Science and Technology Relevant to the Biological and Toxin Weapons Convention: Summary of an International Workshop: October 31 to November 3, 2010, Beijing, China

ISBN
978-0-309-20929-8

56 pages
6 x 9
PAPERBACK (2011)

Katherine Bowman, Kathryn Hughes, Jo L. Husbands, James Revill, and Benjamin Rusek, Rapporteurs; Convened in cooperation with Chinese Academy of Sciences; IAP--The Global Network of Science Academies; International Union of Biochemistry and Molecular Biology; International Union of Microbiological Societies; National Research Council

Trends in Science and Technology Relevant to the Biological and Toxin Weapons Convention

SUMMARY OF AN INTERNATIONAL WORKSHOP

October 31 to November 3, 2010
Beijing, China

Convened in cooperation with

Chinese Academy of Sciences
IAP – The Global Network of Science Academies
International Union of Biochemistry and Molecular Biology
International Union of Microbiological Societies

Katherine Bowman, Kathryn Hughes, Jo L. Husbands, James Revill, and Benjamin Rusek, Rapporteurs

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

THE NATIONAL ACADEMIES PRESS
500 Fifth Street, N.W. Washington, DC 20001

NOTICE: The project that is the subject of this summary was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

This project was supported by the Alfred P. Sloan Foundation, Chinese Academy of Sciences, IAP - The Global Network of Science Academies, U.K. Global Partnership Programme, U.S. Defense Threat Reduction Agency, U.S. Department of State, U.S. National Institutes of Health, and U.S. National Academies. The views expressed herein are those of the authors and do not necessarily reflect the views of the organizations or agencies that provided support for the project.

International Standard Book Number-13: 978-0-309-20929-8
International Standard Book Number-10: 0-309-20929-3

Additional copies of this summary are available from the National Academies Press, 500 Fifth Street, N.W., Lockbox 285, Washington, D.C. 20055, (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area); Internet, http://www.nap.edu.

Printed in the United States of America.

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

The **National Academy of Sciences** is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Ralph J. Cicerone is president of the National Academy of Sciences.

The **National Academy of Engineering** was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. Charles M. Vest is president of the National Academy of Engineering.

The **Institute of Medicine** was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Harvey V. Fineberg is president of the Institute of Medicine.

The **National Research Council** was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Ralph J. Cicerone and Dr. Charles M. Vest are chair and vice chair, respectively, of the National Research Council.

www.national-academies.org

PREFACE AND ACKNOWLEDGMENTS

The summary presented here provides the rapporteurs' factual synopsis of plenary presentations delivered at the workshop *Trends in Science and Technology Relevant to the Biological and Toxin Weapons Convention*, held 31 October – 3 November, 2010 at the Institute of Biophysics of the Chinese Academy of Sciences and convened under the auspices of IAP – The Global Network of Science Academies, the International Union of Biochemistry and Molecular Biology (IUBMB), the International Union of Microbiological Societies (IUMS), the Chinese Academy of Sciences, and the U.S. National Academies. It does not necessarily reflect the views of members of the Committee on Trends in Science and Technology Relevant to the Biological Weapons Convention: An International Workshop or the National Research Council.

This workshop summary has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published summary as sound as possible and to ensure that the summary meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this workshop summary:

Ronald Atlas, *University of Louisville, United States*
Lorna Miller, *Defence Science and Technology Laboratory, United Kingdom*
Kathryn Nixdorff, *Darmstadt University of Technology, Germany*

Although the reviewers listed above have provided many constructive comments and suggestions, they did not see the final draft of the workshop summary before its release. The review of this report was overseen by **James LeDuc**, *University of Texas Medical Branch at Galveston*. Appointed by the National Research Council, he was responsible for making certain that an independent examination of this summary was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this summary rests entirely with the authors and the institution.

The rapporteurs particularly wish to thank the plenary speakers of the workshop, who were provided with the opportunity to review and comment on the brief factual summaries of their presentations.

CONTENTS

SUMMARY

INTRODUCTION

This document offers a summary of the substantive presentations during an international workshop, *Trends in Science and Technology Relevant to the Biological and Toxin Weapons Convention,* held 31 October – 3 November, 2010 at the Institute of Biophysics of the Chinese Academy of Sciences. It is meant to provide scientists and other technical experts with factual information about the range and variety of topics discussed at the workshop, which may be of interest to national governments and non-governmental organizations as they begin to prepare for the 7th Review Conference of the Biological and Toxin Weapons Convention (BWC) in 2011. The more extensive final report being prepared by an international committee under the auspices of the National Research Council (NRC) of the U.S. National Academy of Sciences (see below) will be published soon. The final report will incorporate the factual material contained in this summary, include additional detail about the "state of the science" for some of the topics covered by the workshop, discuss the potential implications of scientific advances for both the scope and operations of the BWC, and present the committee's findings and conclusions.

The Beijing workshop reflected the continuing engagement by national academies, international scientific organizations, and individual scientists and engineers in considering the biosecurity implications of developments in the life sciences and assessing trends in science and technology (S&T) relevant to nonproliferation.[1] The workshop was planned by an international committee appointed by the NRC and convened in collaboration with IAP – The Global Network of Science Academies, the International Union of Biochemistry and Molecular Biology (IUBMB), the International Union of Microbiological Societies (IUMS), and the Chinese Academy of Sciences. The statement of task for the project may be found in Box 1; the members of the committee, the workshop agenda, and the participant list are included in the Appendix to this summary.[2]

[1] A discussion of previous engagement by the life sciences community can be found in Chapter 1 of the *2nd International Forum on Biosecurity: Report of an International Meeting, Budapest, Hungary, March 30-April 2, 2008* (NRC, 2009a) and a list of activities undertaken by national science academies and international scientific organizations is also available in Appendix C of *Challenges and Opportunities for Education About Dual Use Issues in the Life Sciences* (NRC, 2011a).

[2] This material, as well as copies of many of the PowerPoint slides used by the speakers, is also available online at http://dels.nas.edu/Past-Events/Trends-Science-Technology-Relevant/DELS-BLS-09-06.

BOX 1
STATEMENT OF TASK

An ad hoc committee with significant international membership will be organized by the NRC to:

• Plan an international workshop to survey key trends in areas of science & technology (S&T) that might be potentially relevant to the development of new or more deadly biological weapons and/or to developments in detection, diagnostics, therapeutics, or vaccines that could affect potential prevention and response to biological attacks. The developments in science discussed at the workshop are likely to be in areas such as immunology, neuroscience, synthetic biology, aerosol and other controlled delivery mechanisms, or others; the specific S&T areas and trends to be discussed during the workshop will be selected by the committee.

• Prepare a report of the workshop that would provide findings, based on the consensus of the committee, about the state of the science in the topics discussed at the workshop. The report will also explore potential implications for the Biological Weapons Convention as an independent input from the scientific community to the treaty's 7th review conference in 2011. The report would not make recommendations about actions to address any of the potential implications.

• A rapporteur-authored summary of the workshop plenary sessions will also be produced.

The workshop provided an opportunity for the scientific community to discuss the implications of recent developments in S&T for multiple aspects of the BWC. For example, a continuing question for the treaty's review conferences is whether scientific developments yield new or novel types of agents or materials that are not captured by Article I, which defines the scope of the treaty?[3] More broadly, however, developments in S&T also affect the other key articles of the convention that provide for the operation of the treaty, such as the adequacy of national implementation of the convention through national policies and regulatory systems, the capabilities to carry out investigations of alleged use of biological weapons, and the design of international cooperation to ensure that all States Parties (i.e., those who have signed and ratified the agreement), have access to the benefits of peaceful applications of biology.

[3] Article 1 includes "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" (http://unhq-appspub-01.un.org/UNODA/TreatyStatus.nsf/44e6eeabc9436b78852568770078d9c0/ffa7842e7fd1d0078525688f0070b82d?OpenDocument). An account of decisions taken at various review conferences reaffirming the capacity of Article 1 may be found at http://www.unog.ch/80256EDD006B8954/(httpAssets)/699B3CA8C061D490C1257188003B9FEE/$file/BWC-Background_Inf.pdf.

The summary follows the structure of the plenary sessions at the workshop. It begins with introductory material about the BWC and current examples of the types and modes of science advice available to the BWC and other international nonproliferation and disarmament agreements, in particular the Chemical Weapons Convention (CWC). The S&T material begins with talks on areas having the potential to impact the design, fabrication, and production of biological weapons, continues with a session on dispersal science and delivery technologies, and next moves into scientific developments relevant to detection, identification, and monitoring. Later sections of the workshop focused on medical countermeasures, public health, and agricultural biosecurity, and finally conclude with presentations on ways in which new methods of collaboration are influencing scientific exchange along with a discussion of risk communication. The summary includes only a very brief description of the some of the post-presentation discussions held during the plenary sessions – and does not include an account of the smaller breakout groups – since these were intended to inform the committee's findings and conclusions and will be reflected in the final report.

By necessity, the workshop was able to present only a sampling of current research in relevant areas of science and technology, and was strengthened by being able to draw on the diverse perspectives and active engagement of the participants through both plenary and breakout discussion sessions. Almost 80 scientists and policy makers from 28 countries and several international organizations took part in the workshop, with a mix of scientists and engineers currently engaged in research and technical experts who could help draw out potential implications for the BWC. The speakers for the S&T sessions were asked to focus on the "state of the science" with regard to their topics; in a few cases they also offered additional comments on the implications and applications for the BWC.

INTRODUCTION TO THE THEMES, GOALS, AND CONTEXT OF THE WORKSHOP

Outline of the Aims and Objectives of the Meeting – Roderick Flower, Queen Mary University of London, UK

Dr. Roderick Flower, chair of the Committee on Trends in Science and Technology Relevant to the Biological Weapons Convention: An International Workshop, welcomed participants to the meeting and noted that the review conferences of the Biological and Toxin Weapons Convention have been charged with taking into account new developments in science and technology. Accordingly, Dr. Flower noted that the mission

for the workshop was to review and consider developments in areas of science and technology that might be relevant to the Convention, in order to provide independent input from the scientific community to help inform the 7th Review Conference preparations. Dr. Flower then briefly reviewed the agenda and structure of the meeting.

The Biological Weapons Convention: A Brief Overview – Piers Millett, BWC Implementation Support Unit, United Nations

Dr. Piers Millet of the BWC Implementation Support Unit opened his remarks by reviewing the basic provisions of the BWC and its modest organizational resources (a staff of three) relative to the other major nonproliferation agreements. He noted that the BWC continues to evolve, becoming more collegial, more informal and more representative in many of its activities, particularly through the development of the intersessional process.[4] Dr. Millet emphasized the ways in which the BWC has sought to engage the broader community of stakeholders interested in issues of potential misuse, including scientists and engineers. He commented on the need for the BWC to be better connected to developments in modern life sciences and to be part of a larger context of responsible conduct of science. He noted that the BWC was interested in several potential contributions from S&T developments, both positive and negative: to the risks of new or more deadly weapons; to improved defenses and countermeasures; and to enhanced disease surveillance and response.

Dr. Millet pointed to efforts by the international scientific community to contribute to discussions on these issues through forums and workshops, as well as through the participation of scientists as delegates, guests, and representatives of non-governmental organizations at official BWC meetings. He closed by encouraging the community to continue its engagement on topics relevant to the BWC, such as advances in science and technology, particularly in support of evidence-based decision making. Although the formal process of the 7th review conference will be largely state-driven, there will be opportunities for events such as the workshop to make a contribution both to preparations by both national governments and the BWC staff's own efforts.

[4] The Review Conferences of the BWC are held at five year intervals. After the efforts to negotiate a verification protocol collapsed in 2001, the States Parties agreed to a series of annual, intersessional Meetings of Experts and Meetings of States Parties on specific themes. The success of the first series led the 6th Review Conference to agree to a second series from 2007-2010, including national implementation (2007); biosafety and biosecurity measures along with oversight, education, and awareness raising (2008); disease surveillance and containment (2009); and assistance and coordination in cases of alleged use (2010). Further information is available from the United Nations' Biological Weapons Convention website at http://www.unog.ch/bwc.

Framework for Evaluating New Science and Technology – Ralf Trapp, CBW Consultant, France

Dr. Ralf Trapp continued the theme of the first session by pointing to the importance of non-proliferation treaties regularly considering how advances in science and technology might affect their scope as well as their operations. S&T reviews are undertaken by the States Parties of the different agreements, working through international treaty organisations (if they exist) as well as formal treaty mechanisms such as review conferences. The reviews are supported by input from additional sources such as formal scientific advisory panels, such as the Scientific Advisory Board of the CWC and external actors such as scientific unions and academies, industry associations, and nongovernmental organizations (NGOs). He noted that the 7th Review Conference of the BWC has specifically been charged with considering "new scientific and technological developments relevant to the convention."[5]

Dr. Trapp drew comparisons between the BWC and the CWC in how relevant scientific advice has been sought and provided, with a key difference that the CWC has a formal Scientific Advisory Board (SAB) charged to provide advice to the Director General of the Organization for the Prohibition of Chemical Weapons (OPCW). Dr. Trapp provided several examples of independent S&T advice in the context of these two treaties, noting that the OPCW had twice asked the International Union of Pure and Applied Chemistry to carry out workshops on trends in S&T similar to the Beijing workshop because it felt the need for access to a wide array of information from an independent scientific body. He cited a number of reasons for encouraging communication between the BWC States Parties, treaty staff, and the S&T community:

- The pace and complexity of advances in the life sciences;
- The need for connections with cutting-edge science and technology;
- The authority and independence of the advice that the S&T community could provide;
- The importance of feedback into the scientific community on issues relevant to the treaty's operation (e.g., on issues such as awareness raising, adoption of codes of conduct, education); and
- The importance of engaging the S&T community in the development of governance measures.

[5] The mandate for the 7th Review Conference is available at http://www.unog.ch/80256EE600585943/(httpPages)/57A642B96534F50CC12577B5004DD75E?OpenDocument.

Perspective from the Chinese Academy of Sciences – Li Huang, Institute of Microbiology, Chinese Academy of Sciences

Dr. Li Huang provided a perspective from the Chinese Academy of Sciences (CAS). He noted that China has a long history of S&T developments and provided information on the Chinese Academy of Sciences' role as a leading life sciences research institution. Dr. Huang pointed to previous engagement by the Academy in discussing ethics and integrity in science and promoting ethical conduct. He highlighted several recent activities including the establishment of a Center for Ethical Studies in Science and Technology (2005), participation in the IAP Biosecurity Working Group, the Declaration of Scientific Ideology (2007), and CAS participation in international workshops and roundtables. Although he noted challenges such as a lack of awareness about the dual-use potential of scientific research among members of the life sciences community, he observed that scientists in China were actively engaged in discussing biosecurity issues and considering what oversight measures might be appropriate to manage potential risks.

Discussion

The discussion following this session's presentations touched on ways to make independent input from the scientific community useful to the policy and diplomatic communities of the BWC, as well as ways one might measure the impact of meetings such as the current workshop. For example, some participants noted that producing a relatively brief and accessible summary of the final report would be helpful to convey the key findings and conclusions to the diplomatic and policy communities engaged with the BWC.

DEVELOPMENTS IN DESIGN, FABRICATION, AND PRODUCTION

Bioinformatics and Computational Tools – Etienne de Villiers, International Livestock Research Institute, Kenya

Dr. Etienne de Villiers opened the session with a discussion on the potential of bioinformatics and computational tools. He began by noting that he had never considered the use of his research for offensive weapons development, and rather considered bioinformatics a useful tool for assisting with areas such as vaccine development. Indeed, bioinformatics is useful in enhancing understanding of genome structures and in enabling the identification and manipulation of genes to make clear their functions. To accomplish

this, bioinformaticists use an interdisciplinary approach that combines biology with statistics, mathematics, algorithms, databases and text mining.

Dr. de Villiers pointed out that there had been a genomics revolution over the last couple of years resulting in next generation sequencing which exploited the latest technology to achieve millions of sequences an hour. This technology is advancing rapidly—whereas the Human Genome Project cost hundreds of millions of dollars or more and took a great deal of time, it is now possible to sequence a genome in a week for thousands of dollars—resulting in an explosion of genome data.[6] By means of examples, he pointed to the international 1000 genomes project, which involves looking at 2500 human genomes for genetic variation, and the 1000 plant and animal genomes reference project conducted by BGI China.[7]

Dr. de Villiers went on to outline how an explosion in computing power, in combination with lowered costs for computers and greater availability of this technology across the globe, is enhancing bioinformatics. These changes have resulted in the emergence of the concept of cloud computing, whereby individuals can gain legitimate access to high performance computers through the internet to conduct research. Under this model, computational power is a service that can be rented by users to the extent needed to achieve research goals. An alternative approach, termed distributed computing, draws from a network of smaller computers to create a supercomputer-like environment that enables analysis of complex problems. One example is the "Folding@Home" project which has a goal "to understand protein folding, misfolding, and related diseases."[8] Individual participants can donate a portion of their idle computer processing power to the analysis of protein structures. Dr. de Villiers noted that in 2009 40,000 central

[6] The Human Genome Project cost several billion dollars (The Human Genome Project Completion: Frequently Asked Questions, available at http://www.genome.gov/11006943), which included more than technology and sequencing expenses. Several companies currently offer human whole genome sequencing services and the prices continue to drop. Illumina, Inc., for example, offers genome sequencing for $19,500 with sequencing in "medically indicated cases" costing $9,500 (www.everygenome.com; accessed 3/14/2011). Similarly, whole genome sequencing by Complete Genomics reportedly costs approximately $10,000 (http://www.completegenomics.com/) and the company has reported its sequencing consumables costs to be approximately $4,400 (Drmanac et al., 2010). Companies continue to pursue advances in technology and to decrease sequencing costs as they race toward a "one thousand dollar genome", which has been seen as an important milestone below which demand for genome data is expected to explode still further (Wolinsky 2007; Venter 2010).

[7] Information about the 1000 Genomes Project may be found at http://www.1000genomes.org and the 1000 Plant and Animal Genomes Reference Project at http://www.ldl.genomics.cn/page/pa-research.jsp.

[8] Information on Folding@Home is available at http://folding.stanford.edu/.

processing units (CPUs) supported this project, making it in essence the largest computer in the world.[9]

Advances in computational power and performance have resulted in 'metagenomics', an example of which is the Sargasso Sea community survey (Venter et al., 2004). Dr. de Villiers defined metagenomics as "the sequencing and analysis of DNA of organisms recovered from an environment, without the need for culturing them, using next generation sequencing technologies" and suggested that metagenomics could play an important role in global disease tracking as it enables researchers to identify and track what exists and where pathogen reservoirs are located. Over time this could facilitate the development of diagnostic sequencing capabilities and understanding of disease trends, or even the production of vaccines and drugs. To begin this process Dr. de Villiers and colleagues at the International Livestock Research Institute had begun the process of building a biobank to manage samples, which he suggested could be a unique resource for other researchers to use.

Systems Biology – Andrew Pitt, University of Glasgow, UK

The second speaker in the session was Dr. Andrew Pitt of the University of Glasgow, who discussed the issue of systems biology. Dr. Pitt began by pointing out that systems biology had become a buzzword for a process of using biological knowledge to produce a mathematical model that describes a system at different levels from the molecular to the ecosystem. Such a model could not only describe the system, but could be used to enable the researcher to make system predictions. In this regard, systems biology lies in the middle ground between informatics and synthetic biology and provides the resources to enable the conversion of biological information into something meaningful from which to generate new systems and biology.

Dr. Pitt noted that this is achieved by taking a rational engineering approach which draws from systems engineering and mathematics, along with increasingly diverse approaches to understanding systems including mobile phone networks and traffic management. Using these approaches, researchers have sought to take biological information and convert it into a suitable format from which to build a discrete model that can be described mathematically. Such a model can be used to both describe but also to predict. The latter is particularly important and requires the development of specific models to test predictions, something which becomes more complex as the focus shifts from cells,

[9] The central processing units of a computer are involved in carrying out the instructions in a computer program; depending on the nature of the problem to be solved, the number of CPUs may provide an indication of computing power.

to tissues, to organisms, and to ecosystems. Indeed, the development of models which account for the relationship between these different levels and scales of complexity is particularly challenging and as a unified science, systems biology has a long way to go.

Nonetheless, current research generates the potential to achieve systems medicine in the future and there are a number of enabling technologies, such as genomics and proteomics, which have facilitated progress. Coupled with these developments, advances in mass spectrometry and high throughput screening provide the depth of data required to populate models while the increased understanding of bioinformaticists enables such data to more effectively be captured and converted. Though some of the underlying networks are relatively straightforward and there are key nodes where we can intervene, the complexity of connections nonetheless renders systems biology a challenge, evident in an example from Japan articulating the epidermal growth factor receptor (EGFR) signaling cascade, which illustrates the relationship between proteins and other elements within a systems pathway (Oda et al., 2005).

Dr. Pitt went on to elaborate on why a key challenge for systems biology is solving the mathematics, which in the case of the EGFR pathway model requires addressing some 211 reactions in 322 components, forming 7 RNAs based on 202 proteins, and the calculations here only cover a small portion of the mapping process. To understand how the complete system works, a massive number of interactions must be examined: at the genetic level it is likely to require some 4,000 calculations with a further 5,000 calculations at RNA level and 50,000 interactions in one mathematical equation at the level of proteins. In this regard, Dr. Pitt suggested that the number of numerical parameters is one of the main limits to advances in systems biology, particularly given that biological data reduction is slow and expensive and computational power is limited because of scale.

A further challenge identified by Dr. Pitt was the difficulty in overcoming the stochastic nature of some of the interactions, which is difficult to model using mathematics. He then elaborated on the potential for an approach which focused on building platforms to generate data more quickly. He noted, however, that even this approach still requires advances in computational power, and that while this is improving, there is still some way to go to achieve the improvements required to build substantial models and intervene at the cellular level.

Emerging Trends in Synthetic Biology – Pawan K. Dhar, University of Kerala, India

Dr. Pawan Dhar of the University of Kerala discussed emerging trends in synthetic biology in the third presentation of the session. Dr. Dhar began by pointing out that there was enormous possibility of creating useful applications using a rational design approach in biology. Accordingly, he suggested there was a need for building standards and rules of composition to engineer novel biological applications. Dr. Dhar said that in contrast to the top down traditional approach, the engineering "bit by bit" strategy focused on the composite sections of the system to create useful devices and networks.

He observed that scientists learnt biology by making 'junk' (mutations, knockdowns) and 'garbage' (knockouts) out of genes. He asked if one could do the opposite, i.e., make genes out of 'junk' DNA. His work has led to the effective conversion of "junk sequences into genes", with the 'junk' being non-protein-coding genes within a genome. Dr. Dhar presented an example of E. coli research to illustrate this approach, where six intergenic sequences with no history of transcription were artificially activated to code for proteins (Dhar et al., 2009). His research indicated that although most of the gene activations had little or no effect on cell growth, activating one of the intergenic sequences resulted in cell death. Subsequent deactivation of this gene restored cells to normal growth, although why this happened was unclear at the molecular level. Further, given that a DNA sequence could now be artificially expressed in several frames, he proposed the emergence of combinatorial genomics as a new way of doing biology.

Dr. Dhar then described some of the outreach work being conducted at the Centre for Systems and Synthetic Biology, in India. The Centre recently organized Biodesign India, the first synthetic biology event in the country. The aim was to try and understand what bio-design related activities were underway in India and address a degree of sensitivity to the surrounding ethical questions of this type of research. To provide an open access platform for synthetic biology research in India, the Centre has set up a synthetic biology wiki (a webpage that enables users to create and edit content) for information sharing among labs.

On the global stage, Dr. Dhar suggested that in the future we were going to see arrival of faster and cheaper DNA synthesis technologies and cited the work of Robert Carlson, who recently predicted rapid fall in the cost of long DNA synthesis (Carlson, 2009) and Craig Venter, whose group experimentally developed a "synthetic" microbial cell

(Gibson et al., 2010).[10] He pointed out that Dr. Venter's approach was prohibitively expensive and time consuming, and thus not likely "scalable" in the present form. However, Dr. Dhar predicted that rapid and cheaper organism construction strategies, whole genome cloning, synthetic chromosomes, and application-oriented minimal synthetic cells would emerge in future. Dr. Dhar suggested that ideas like non-natural genetic codes, RNA structural engineering, and computer aided design of pathways may be more accessible and he envisions the emergence of several major non-biobrick initiatives in the near future.[11] He also predicted a trend toward a greater number of graduate programs (Masters and Ph.D.) in synthetic biology worldwide. He observed that due to lack of experience in constructing organisms it was difficult to accurately predict the potential adverse effect of this approach, and noted that it makes him nervous to visualize the scenario of someone firing microbes as bullets, given the fact that such bullets think. As a result, he concluded by noting that it is not possible to maintain absolute control over developments in the biological sciences such as synthetic biology, but that "big challenges, [an] unclear roadmap, [and a] fear of the unknown" remain.

Discussion

The session moved to an open discussion during which a number of key themes emerged. Many participants noted that our knowledge and understanding still remains limited in terms of an ability to predict the outcomes and functions of biology resulting from genetic modification or modulation. Accordingly, the challenge of developing appropriate risk assessment strategies to accommodate unpredictable systems is difficult. Equally, participants suggested that it would be difficult to regulate the things "we don't know that we don't know", although participants pointed to the value of bringing together the science and policy communities to discuss these issues. Finally, participants noted the continuing worldwide expansion of biological sciences research capacity, such as the active synthetic biology community in India and the ability of research institutes in Kenya to draw on advanced computational resources.

[10] As described in the cited article, Dr. Venter's group chemically synthesized the genome of the bacterium *Mycoplasma mycoides* based on the genetic sequence of the naturally occurring organism with the addition of certain distinguishing chemical "watermarks" and inserted this synthesized genome into a recipient cell of the related bacterium *Mycoplasma capricolum*, from which the natural genetic material had been removed. The synthesized *M. mycoides* genetic material was successfully able to instruct the resulting cell to grow and self replicate (Gibson et al., 2010).

[11] The bio-brick model seeks to create standardized DNA "parts" with defined functions for combination into new systems. More information is available through the BioBrick Foundation at http://openwetware.org/wiki/The_BioBricks_Foundation and the Registry of Standardized Biological Parts, available at http://partsregistry.org/wiki/index.php/Main_Page.

DEVELOPMENTS IN DESIGN, FABRICATION, AND PRODUCTION, CONTINUED

Bioreactors and Transgenic Animals – Ryszard Słomski, Poznań University of Life Sciences, Poland

Dr. Ryszard Słomski opened the session with a discussion on bioreactors and transgenic animals. He began by highlighting the importance of working with a group of experts in a variety of sub-disciplines in order to achieve success. Dr. Słomski continued by outlining a number of systems for transgenesis, and noted that effective research requires the difficult decision of which specific system will be best for a particular application. Agreement on the most suitable selection of protein for production, the most suitable targeted site of transgenesis, and the most appropriate organism for transgenesis is also necessary. Dr. Słomski identified other considerations that must be taken into account in selecting transgenesis systems, including required production yield, processing, utilization of the recombinant product, and time. He noted that multiple classes of polypeptides may be produced in such bioreactors, including growth factors, hormones, enzymes, immunoglobulins, and others.

Dr. Słomski then proceeded to highlight a number of key examples of animal bioreactors, including silkworms, rabbits and goats. He posited that the silkworm is a particularly useful bioreactor because of the productive capacity of the silkworm's silk gland, ease of harvesting the product from the cocoon, and relative ease with which transgenesis can be achieved. Rabbits were a second example cited as useful because of their capacity for milk production, which can reach as much as two liters of milk per lactation and which can be manipulated to produce secreted protein (Lipinski et al., 2003). Similarly, goat's milk can be used to produce a recombinant form of human antithrombin, and indeed Dr. Słomski noted that this was the first transgenically produced protein approved for human use in the world.[12] He also described work being done to "humanize" pig tissue to make it available for use for organ and tissue transplants.

Dr. Słomski proposed that there were a number of advantages to the exploitation of animal bioreactors including the fact that such bioreactors exhibited high efficiency of expression, although this is not currently controllable, and required comparatively low maintenance costs. There are also disadvantages, namely the time required for development of the transgenic animal and the chance that the genetic modifications may not pass through to the second or third generation. This latter problem can be countered

[12] ATryn®, produced by GTC Biotherapeutics (http://gtc-bio.com).

by introducing cloning of animals, though this does bring with it a new set of challenges.[13] With respect to the potential impact of research on transgenic animals and the BWC, Dr. Słomski noted that work in this area is tightly controlled and regulated.

Transgenic Plants and Recombinant Pharmaceuticals – Julian Ma, St. Georges University of London, UK

Dr. Julian Ma began the second presentation by positing that molecular pharming–the use of plants as factories for recombinant pharmaceutical proteins–offered an unprecedented opportunity to produce valuable molecules economically and on a massive scale. It was suggested that following the initial genetic manipulation, the process of growing and harvesting the target pharmaceutical protein was essentially low-tech and amenable to facilities around the world. Moreover, new plant biotechnologies had brought about enormous improvements in terms of speed and once the process was initiated the product could be manufactured within two weeks. A number of advantages to this approach were identified as important:

- Plants cells are eukaryotic, like human cells, and can produce complex proteins. Although plant and animal glycosylation patterns differ, engineered removal of the non-mammalian sugars can achieve very homogenous glycosylation patterns.
- Plants are the only feasible production system for some proteins that are required at massive scale.
- Some plant biotechnologies are unparalleled for speed of production
- Low cost of initial investment and economy of scale
- A low-tech "high-tech" solution–readily transferred to under-developed regions
- The prospect of minimal processing for mucosal delivery

Dr. Ma went on to illustrate the advantages of molecular pharming using the example of monoclonal antibodies, highly valuable proteins that are important in both prophylaxis and treatment of disease. Molecular pharming in plants has already produced a number of important monoclonal antibodies, including antibodies directed against HIV, rabies virus, and *Streptococcus mutans*, and it was suggested that such antibodies can potentially be mass produced for a low cost (Ma et al., 2003; De Muynck et al., 2010).

The presentation moved on to point out that antibodies produced in plants could not only be used to combat diseases, but could also serve as biosensors for detection of microbial toxins. Early progress has been made in this field, and Dr. Ma suggested that the

[13] Examples include Skrzyszowska et al. (2006) and Skrzyszowska et al. (2008).

important next step will be to link the plant-expressed antibody to a plant signaling cascade to send a signal when the antibody receptor is bound by its target. In concluding slides, Dr. Ma illustrated how minimally processed plant tissue could serve as a source for the generation of vaccine stockpiles. He presented the example of vaccine antigens for Hepatitis B, which were expressed in potatoes and then delivered through feeding. The process resulted in significantly increased antibody levels in human volunteers, which far exceeded the level required for immunity.[14] Such a process, it was suggested, could be applied to a number of other disease examples, and the use, for example, of plants seeds, a natural protein storage structure, would enable stockpiling of unprocessed vaccine in large quantities under standard agricultural conditions.

He concluded that although the field of molecular pharming was still young, excellent progress was being made and the first products were in clinical trials. In the future, it was hoped that further significant improvements in yields and speed of production could be achieved.

Neuroscience Developments – James Eberwine, University of Pennsylvania School of Medicine, USA

Dr. James Eberwine of the University of Pennsylvania began by pointing out that the brain affects a range of characteristics, including emotions and the ability to learn. He outlined how his laboratory was involved in fundamental science, which was the key to exploiting the beneficial use of biology and understanding its potential for misuse. In particular, Dr. Eberwine explained the complexity of neurobiology, indicating that such work required the development of techniques to allow researchers to more precisely understand function at the single cell level (Eberwine and Bartfai, 2011).

Dr. Eberwine noted that high-throughput sequencing has significantly advanced neuroscience, and suggested that next generation sequencing would enable researchers to achieve a level of 45 billion nucleotides per week. Research has revealed significant variability in RNA and gene expression between functionally similar individual neurons, highlighting the importance of multiple cellular data points. He suggested that one of the key realizations was the need to think about phenotypic space differently. He posited that this space is not homogenous and thus cellular identity does not reflect a particular point, but rather a position on a three dimensional phenotype "cloud" (Sul et al., 2009; Kim and Eberwine, 2010). This cellular variation has serious implications for the use of model systems for a given cell type, which may result in errors in conclusions if one does not understand the specific variations between the model and the studied system. For

[14] An early example of this application includes Thanavala et al. (1995).

example, mRNAs from mouse and rat hippocampal dendritic cells share only 27 percent similarity to each other, which can have serious implications for the observed responses of these cells.

Dr. Eberwine discussed the origins of this variability by using the way that adjusting proportions of common ingredients (e.g., flour, milk, eggs) results in different baked goods (pancakes, cakes, biscuits) as a conceptual model. He noted that cells use the same fundamental components (DNA, proteins, RNA) in different quantities and fashions to create different cellular environments and responses to stimuli. This does not just occur in different types of cells (e.g., neurons vs. astrocytes), but also in cells that appear to be structurally and functionally similar. In particular, Dr. Eberwine noted that RNA is critical in determining the role that a given cell will play in the body, and modification of the RNA profile of a cell allows one to take even differentiated, mature cells, and modify them to perform a different function, such as to turn a neuron into an astrocyte. Manipulation of this cellular plasticity has the potential to reveal fundamental insights into how cells function, to aid in the development of new screening platforms for drug discovery, and potentially to inform the development of personalized cellular therapeutics.

The idea of changing cellular function by insertion of RNA is not a particularly new idea, but the idea of changing the *identity* of a cell through insertion of RNA is rather different. Though not of immediate concern, Dr. Eberwine noted that the plasticity of brain cells revealed through his research could become a dual-use concern in the future. As the beneficial effects to manipulating this plasticity becomes more apparent and within reach, the potential for misuse will also become a possibility.

Discussion

The open discussion following the presentations included additional discussion of the limits and advantages of using plant and animal bio-production systems. For example, issues that were noted by participants included the ability of plants to produce vaccine proteins and monoclonal antibodies, or to be engineered to serve as biosensors, which may have implications for issues of relevance to the BWC in areas such as detection and countermeasures development. Participants also noted that the ability to store plant seeds and to grow plants as needed may influence flexible production capabilities. Participants also inquired about changes of gene expression in neuronal cells, such as those discussed by Dr. Eberwine, and it was noted that while this has been accomplished in sliced sections, *in vivo* application would remain extremely challenging.

DISPERSAL AND DELIVERY

Aerosols and Aerobiology – Chad Roy, Tulane National Primate Research Center, USA

Dr. Chad Roy began the session by discussing infectious disease aerobiology. Although he noted that naturally-acquired infections tend to be characterized by more heterogeneous aerosol size, particle distribution, and temporal patterns than experimentally controlled studies, he pointed out that understanding factors such as environmental susceptibility, aerosol size and distribution, deposition, and interactions in the respiratory system are key to understanding airborne disease processes, whether in natural or experimental contexts (Roy and Milton, 2004). He noted that it is very difficult to study the complex, dynamic system of disease progression through empirical studies alone, and that experimental work is required. Dr. Roy also presented several examples demonstrating that microbial viability in aerosols differed significantly among strains and species, as well as with varying aerosol particle sizes. All of these factors (the physical characteristics of the aerosol, the biological characteristics of the pathogen, the susceptibility of a given individual or population, etc.) play significant roles in determining the eventual progress of the disease.

Dr. Roy described the ways in which deposition within the respiratory tract is affected by the aerodynamic particle size, a characteristic that takes into account particle density. In humans, particles with an aerodynamic diameter of 10-30 micrometers generally deposit in the mouth and nose, particles of 2-10 micrometers deposit in the trachea and bronchi, and particles of less than 2 micrometers reach the alveoli. Particular areas of the respiratory tract can thus be targeted by exposure to differently sized particles, while the tissue susceptibility of different respiratory tract regions to a particular disease agent is also likely to vary. Clearance mechanisms such as exhalation and mucociliary clearance also determine the duration the body is in contact with the agent, affecting the disease pathology.

Dr. Roy led into a discussion of how research on aerobiology has contributed to the development of alternative, inhalation-based methods of drug and vaccine delivery. Inhaled vaccines seek to elicit protective immunity at both the mucosal surface, where exposure to the disease agent would naturally occur, and systemically through the generation of serum antibody titers. Dr. Roy pointed out that research on inhalation delivery is not new, and noted studies on aerosol vaccination against agents of both public health and biodefense significance from the 1950s to 2000s (including Cohn et al., 1958; Tseng et al., 1995; and Sepúlveda-Amor et al., 2002). However, he noted that early

efforts suffered from vaccine reactogenicity, lack of suitable mucosal adjuvants, and limited availability of individual inhalation devices. However, Dr. Roy concluded by presenting data from several recent studies in which advances in the production of subunit vaccines and alternative formulations to prolong residence time have been able to achieve improved efficacy of inhalable biologics.

Nanostructured Delivery Systems for Drugs, Proteins and Cells – Jackie Ying, Institute of Bioengineering and Nanotechnology, Singapore

Dr. Jackie Ying, of the Institute of Bioengineering and Nanotechnology, continued the session by describing some of the components of the "nano tool box" and discussing ways in which nanomaterials with unique properties may be designed to serve purposes such as targeted drug delivery and tissue regeneration.

Dr. Ying reported that formulation into nanoparticles may help protect a protein or drug from systemic degradation and may also reduce side effects by reducing the dosage required and promoting site-specific uptake. Nanosystems may include conjugated molecules designed to bind cell-surface receptors. Temperature-responsive, pH-responsive, and stimuli-responsive systems may also be created through the use of varying polymer subunits and chemical groups. Dr. Ying presented several examples of such engineered polymeric nanosystems, including nanorods designed to release the chemotherapeutic drug Paclitaxel only when exposed to the slightly acidic pH within cancer cells and not when at neutral physiologic pH (Zaman et al., 2010). She also described glucose-sensitive systems in which insulin is released as glucose concentration rises and the free glucose disrupts polymer cross-linking. This system can be designed to be reversible, enabling multiple cycles of polymer dissolution and insulin release, followed by re-formation, as glucose concentration rises and falls, which would allow for much finer control of blood sugar levels than existing treatments.

Dr. Ying next discussed several examples of the use of polymeric scaffolds for tissue regeneration. She presented an example of a nanocomposite constructed of inorganic, bone-like mineral apatite complexed to a bone morphogenic protein, along with the polymer poly(lactic-co-glycolic acid) (PLGA), which releases acidic degradation products. In this system, acidic byproducts from PLGA degradation gradually dissolve the apatite and provide sustained release of the protein, promoting healing in bone defect models. Fibrous polymer scaffolds can also be constructed to help promote the attachment and proliferation of seeded cells for soft tissue regeneration applications (Wan et al., 2006; Tai et al., 2010). Dr. Ying concluded by again noting that nanostructured delivery systems can be engineered to meet the unique needs of various applications.

Remarks: Implications Stemming From Advances in Dual-Use Targeted Delivery Systems – Kathryn Nixdorff, Darmstadt University of Technology, Germany

Dr. Kathryn Nixdorff closed the session by providing commentary on potential implications arising from advances in targeted delivery systems. Dr. Nixdorff noted that targeted delivery systems include both viral and non-viral systems, and she highlighted the fact that systems designed to deliver a biological agent such as DNA or protein effectively to target cells and tissues have many important applications in vaccines, cancer treatment, and other therapies.

Dr. Nixdorff reported that multiple viruses have been explored for use as delivery vectors, including adenoviruses, adeno-associated viruses, vaccinia virus, and lentiviruses. Work on such viral vector systems has led to improvements in targeting to specific tissues, gene transfer and expression levels in those tissues, and vector stabilization from environmental degradation (Liu et al., 2007; Mok et al., 2007; Chalikonda et al., 2008). In addition, several studies have successfully demonstrated viral vector administration through aerosols. Advances in aerosol delivery may lead to improved absorption through the respiratory tract and across the blood-brain barrier along with improved protection of the delivered agents or drugs from environmental stress and other detrimental factors (Medina et al., 2003; Hwang et al., 2007; Suri et al., 2007). Dr. Nixdorff pointed out that nanomaterials such as those described by Dr. Ying can serve as "artificial viruses" (Douglas, 2008) to provide targeted delivery of DNA, proteins, and drugs to cells and tissues. These non-viral systems can help overcome some of the safety, manufacturing and immunogenicity issues associated with viral vectors, although transfection efficiency from non-viral systems remains lower than from viral delivery systems.

Targeted delivery may also be employed to deliver bioregulatory molecules such as fentanyl (Wax et al., 2003), insulin (Gunter and Dhand, 2007), oxytocin (Kosfeld et al., 2005) or orexin (Deadwyler et al., 2007), which can alter the functions of physiologic systems and have previously been delivered in aerosols. Given the complexity of biological systems, however, Dr. Nixdorff noted that it was not always possible to predict the effects of such regulators. She pointed to a passage from the 2006 NRC report *Globalization, Biosecurity, and the Future of the Life Sciences*, which observed that dissemination of bioregulators may be more feasible than in the past due to delivery system advances (NRC, 2006).

Dr. Nixdorff concluded by commenting that the ability to exploit advances in delivery technologies appears most relevant to potential state-sponsored programs due to the need

for expertise, funding, and laboratories equipped to design and develop these systems. She noted that States Parties to the BWC and CWC have a responsibility to continue to consider the biosecurity implications of advances in science and technology and highlighted that the scientists developing targeted delivery systems also have a responsibility to consider potential implications of their work. As a result, Dr. Nixdorff expressed concern that education about dual-use issues has not been widely implemented in the life sciences. A great deal of effort by professional organizations and individuals working from the bottom up has been put into drafting and promoting codes of conduct and education programs with the aim of awareness-raising among life scientists about dual-use issues. However, only governments can require and implement education programs through regulations. Therefore, pressure for successful implementation of these programs would be most effective coming from the top as well as from the bottom.

Discussion

Issues raised during the discussion session included the relative barriers to misuse provided by the importance of tacit knowledge in the application of fields such as aerobiology, and the potential window of opportunity, during the current phase of development of these technologies, for the community to consider effectively their potential implications before the relevant knowledge and skills became more widely available.

DETECTION, IDENTIFICATION, AND MONITORING

Postgenomic Technologies – Andrew Pitt, University of Glasgow, UK

Dr. Andrew Pitt opened the session by providing an overview of the state of technology in genomic analysis. Dr. Pitt introduced the topic by describing three different eras of technology development, the genomic, the post-genomic, and the pre-post genomic. During the genomic era, the development of early sequencing technology provided researchers with the tool to understand the genomic underpinnings of biology. However, early technology was slow and expensive, and these genomic analyses identified some of the limitations of genomics in predicting biological outcome. With the development of tools better able to study proteins, metabolites, and the like, science entered the post-genomic era. Today, Dr. Pitt argued, further advances in analytical technology have allowed for a new level of analysis and have, to some extent, returned us to what he called the pre-post-genomic era.

Recent years have seen major advances in the ability to sequence genes quickly and at lower cost, which allows for high throughput analyses. Today it costs approximately $5000 to sequence a genome, and it is believed that the $1000 genome is on the horizon (see discussion in footnote 6). Dr. Pitt noted that, to date, about 6,500 genomes have been sequenced worldwide which is creating a new challenge—massive amounts of data that we do not yet have the tools to fully analyze.

Beyond sequencing technology, Dr. Pitt noted that within the past five years there have been advances in the ability to do fine analysis of cellular environments. This degree of control allows for analysis of whole cells and of partial cells and has improved both the understanding of cellular components and mechanisms and the understanding of the linkage between the genome sequence and biological outcome.

Looking ahead to the next five years, Dr. Pitt predicted that significant advances would be made towards personalized medicine. Anticipated technological developments to support this include the development of multiplex protein arrays and improved analysis methods. There will be a greater focus on identification and study of biomarkers, and other technological developments will be targeted towards understanding RNA interference (RNAi) and the function of small interfering RNA (siRNA). There will also be an increased ability to perform molecular and physical observations of the role genetics play in organisms. Dr. Pitt noted that these developments are relevant to both Articles I and II of the BWC, with potential applications for detection, identification, and verification.

Bioforensics – Randall Murch, Virginia Polytechnic Institute and State University, USA

Dr. Randall Murch introduced the topic of bioforensics by noting his extensive experience in the area, both as a criminal investigator and as a forensic scientist. He described how, over the course of his career, the role of forensics has shifted from one of last-ditch effort on the part of the investigators to a position of prominence, where the forensic laboratory is brought in early in the process and assists throughout an investigation. Today, if a biological event occurred, forensics would be seen by investigators and leaders as a tool to help answer critical questions such as: what is or was released, who is responsible, where did it come from, what can we know with confidence, and by when?

Dr. Murch noted that in order to understand the role that bioforensics can play in answering these questions, it is important that certain terms be clearly defined. *Forensic*

science is "the application of science in the investigation of legal and policy matters. It consists of analysis and interpretation of physical evidence to determine relevance to events, people, places, tools, methods, processes, intentions, [and] plans." The overall goal of forensic science is to identify and characterize that evidence to aid and direct investigators as they seek to assign attribution, often by narrowing potential sources for the physical evidence. *Attribution* is "the assignment of a sample of questioned origin to a source of known origin to a high degree of scientific certainty." When identifying samples and assigning attribution, Dr. Murch noted that it is critical that analysts have a sample of known origin with which to compare an evidentiary sample and that consistent, systematic, and validated methods be used for the analysis. The science often fills a special investigative role, and the results of a forensic analysis can feed into a broader analysis of all evidence available (from intelligence, investigative information, etc.).

In recent years, the emphasis on forensics within an investigation has grown, and as a result, the expectations and requirements for quality and reliability are increasing. Along with these rising expectations is increased scrutiny on the science used within the judicial system. In 2009, the U.S. National Research Council issued a report stating that forensic science and its performers have been shown or assessed to have significant gaps, shortcomings, and needs in areas such as the scientific basis and validation in some disciplines; the credentials and training of performers; funding and infrastructure; organizational independence; and the understanding, use and scrutiny by legal and judicial communities (NRC, 2009b). Dr. Murch expressed the hope that improvements in these areas will result in greater accuracy and defensibility of the science of forensics, which will in turn support increased confidence in the results of forensic analyses.

Moving to the specific area of microbial forensics, Dr. Murch again emphasized the necessity of consistent analysis methods and for obtaining a sample of known origin for comparison with samples collected as evidence in an investigation. Currently, the analyses used for microbial forensics are very context and situation dependent. There are a large number of pathogens that can negatively affect human, animal, and plant health, and for the vast majority, the appropriate method for forensic analysis has not been worked out or validated. Complicating matters further, there is a large array of genomic, physical, and molecular analytical methods that are available for use, but in some cases, the limitations of those analyses for characterization and identification purposes are not yet clear. In addition, Dr. Murch noted that he expects advances in analytical methodology to continue to occur at a rapid pace, and to provide new opportunities and new questions for forensic science.

In spite of these challenges, Dr. Murch noted that there is great potential for microbial forensics to be a critical tool to assist in the response to and investigation of terrorist attacks or hoaxes, support global non-proliferation efforts, aid in tracking and control of agricultural or public health outbreaks (either natural or of a suspicious origin), and other similar activities. In the future, microbial forensics could be used to help address the potential threats posed by engineered pathogens. However, to achieve its full potential will require the development of robust, effective, validated, and defensible analytical methodologies and the availability of samples of known origin. Since forensics is only effective when part of a broader legal and policy system, Dr. Murch suggested the development of a global, cooperative network in support of biosecurity and the development of a strategy within the BWC framework that could:

- Identify "grand science challenges"
- Establish standards/guidelines for collection, preservation, analysis and reporting and interpretation of results for organisms, toxins and sample types
- Accept quality management standards
- Provide standardized introductory and advanced training, personnel certification protocols for voluntary or selected participants
- Establish one or more accredited UN-authorized microbial forensics laboratories based on international quality management standards, and modus operandi to include transparency
- Establish accepted sample sharing, analysis protocols
- Establish an international microbial forensics repository which leverages existing, related resources, to include specimens which help to describe relevant geotemporal microbial background
- Develop and validate legal & policy requirements for microbial forensics capabilities that support UN--sponsored investigations, and then criteria and guidelines for use of science in UN actions

Trends in Biosensors – Gary Resnick, Los Alamos National Laboratory, USA

Dr. Gary Resnick began his talk by providing a general overview of biosensors as an analytical device designed for detection, and sometimes identification, of a biological analyte. Biosensors contain three key components: a biologically sensitive element, a transducer, and a signal processor. There are many available variations of these elements, some based on recognition (binders, protein engineering, etc.) and some based on transduction (electrochemical, optical, etc.) (Luong et al., 2008). These detectors are found in many areas including public health, agriculture, food safety, and security. Today, most biosensors can be found in central laboratories. In the future, Dr. Resnick

hypothesized that detectors will become portable and more available for on-site, field-based analysis.

Encouraging the development of new biosensors, Dr. Resnick described the pull of societal needs, such as climate change and increased food production, and the push of new technology opportunities provided by the convergence of diverse technological developments in engineering and biological sciences and the drive for high-throughput bioanalysis systems. Dr. Resnick speculated that these developments are likely to see a growth and improvement of biosensors and, especially when coupled with advances in the area of systems biology, a veritable tsunami of biological information that will be a significant challenge to manage and process. In particular, he highlighted two advances that would be transformational for the field: the development of handheld biosensors and the development of "dipstick" technology—very simple-to-use, inexpensive sensors.

Advances in materials science, bioengineering (synthetic ligands, etc.), high-throughput genetic screening methods, and other fields will likely result in the development of new, faster assays, novel sensor platforms, and more efficient use of materials and reagents, perhaps even with the development of more robust, hand-held, self-contained detectors. However, no single biosensor will be able to address the requirements for all fields, and the development of biosensors in the future will require consideration of the need it is designed to meet. For example, a system designed for biodefense purposes will likely put greater emphasis on portability and high sample throughput than a system designed for diagnostic purposes for the public health arena. Dr. Resnick observed that creating an integrated biosurveillance system that effectively incorporates biosensor-acquired data will also require the development of an iterative process that uses available data streams, information and knowledge management, and knowledge of applications to identify and develop technology to meet to changing needs. Finally, Dr. Resnick emphasized that biosensors may be designed to detect known threats, even a broad range of known threats, but it should be understood that this does not provide absolute detection capability, and new threats or unexpected technological developments should not be a surprise. Biosensors are only part of a larger response and information infrastructure to protect against biological threats, whether naturally or intentionally introduced.

Biosensor Development – Ilya Kurochkin, M.V. Lomonosov Moscow State University, Russia

Dr. Ilya Kurochkin, from Lomonosov Moscow State University (MSU), provided participants with an overview of biosensor development efforts at his institution. The research is in the following areas: scanning probe microscopy for detection and

identification of toxins and microbiological objects; development of an electrochemical bioanalytical platform; development of silicon nanowire transistors; and creation of a lateral flow device with surface-enhanced Raman spectroscopy (SERS) and enzymatic metallography amplification.

First, Dr. Kurochkin described the development of an antigen-antibody binding technique for improved scanning probe microscopy of proteins. In this method, a polymer layer containing antigens for a given biological species is created on a surface. Incubation of this material with the analyte allows for selective aggregation of proteins on the surface of the polymer. These can then be counted directly using scanning probe microscopy. He reported improved analytical sensitivity with this technique than with other methods and applicability to large proteins (over 8 nanometers).

Second, Dr. Kurochkin discussed the development of two analytical methods that lend themselves to use in array-based detectors: electrode-based sensors and silicon nanowire transistors. The electrode-based sensor array can be used for monitoring of neurotoxins and biological species. In this method, manganese dioxide (MnO_2) nanoparticles are placed on the tip of an electrode and run through a series of alternating solutions and washes to create ionized monolayers on the surface. These monolayers can be created to be sensitive for specific compounds of interest and, when exposed, their reaction will cause changes in the current passing through the electrode. These changes can be detected and amplified when incorporated into a detector system. To provide multiplex capability, electrodes can be primed with different solutions and placed in an array. Dr. Kurochkin noted that these systems are currently in use for monitoring and testing in blood analysis and for detection of chemical weapons. He also noted the potential benefit that self-assembly methods have for creating large numbers of low-cost, reproducible sensors for a variety of applications. Next, Dr. Kurochkin described the development of silicon nanowire transistors for high sensitivity detection of ions in solution. By carefully placing a solution droplet onto the transistor one can monitor the affinity of the ions in solution to the transistor by changes in the current through the transistor. As a result, these can be used as detectors for solutions with very low concentrations of analyte.

Finally, Dr. Kurochkin described some advances in the area of surface-enhanced Raman spectroscopy (SERS), a non-destructive, optical technique often used for the study of biological systems. This is a powerful technique, but has low sensitivity, in part due to high background signals from samples. One method for increasing sensitivity is to put the sample on a metal surface, which enhances the Raman signal. It is not uncommon today to use metal nanoparticles to provide the enhancement. At MSU, improved methods for creating thin films of nanoparticles have been developed to improve SERS signals. In

addition, improved sensitivity has been demonstrated by combining nanoparticle-based SERS analysis with a lateral flow device.

Remarks: Science Used in Identifying the Anthrax Mailings – Nancy Connell, University of Medicine and Dentistry of New Jersey, USA

Dr. Nancy Connell, from the University of Medicine and Dentistry of New Jersey, presented an overview of the 2001 anthrax attacks and the subsequent FBI investigation. She noted that during September and October, 2001, seven letters were mailed to media and senate offices in New York, Florida, and Washington DC, leading to contamination of 35 postal facilities and mailrooms, 22 cases of anthrax infection resulting in 5 deaths, and the treatment of 10,000 people judged to be potentially "at risk" with medical prophylactics. The subsequent investigation included the cooperation of 29 laboratories and the collection of 5,730 environmental samples taken from 60 sites. Dr. Connell highlighted some of the scientific techniques used during the investigation, including forms of microscopy to identify physical characteristics of the mailed spores, and forms of spectroscopy to identify chemical composition of the materials. In particular, she noted that the anthrax strain used in the mailings was determined to be the "Ames" strain and that genetic analysis was conducted to identify rare mutations in the mailed spores. Genetic screening was then undertaken to compare these mutations with the genetic sequences of reference anthrax samples from 15 domestic and 3 overseas laboratories. The presentation provided context for an ongoing National Research Council study that was examining the science behind the techniques used to identify the origin of the anthrax spores. Dr. Connell presented the statement of task for the committee and summarized the findings of the public FBI report on the investigation. As the NRC committee's work was ongoing at the time of the workshop, Dr. Connell was unable to present any findings from that study.[15]

Discussion

The discussion that followed highlighted some of the challenges of using detectors alone to monitor for disease outbreak or potential attack. These include the size of detectors; the cost of broad sampling, whether environmental or in a public health setting; the cost and time required to process many samples; observing an emerging signal above the noisy microbial background; lack of availability of known samples for comparison purposes; and the difficult balance between creating a system designed to monitor for a

[15] The report, *Review of the Scientific Approaches Used During the FBI's Investigation of the Anthrax Letters* (NRC 2011b), has subsequently been published and is available at http://www.nap.edu/catalog.php?record_id=13098.

specific threat versus one designed to monitor for a broad range of microbes. Many participants expressed the general sense that significant progress has been made in this area in recent years, and the development of hand held detectors and reduced sequencing costs could result in greater availability of microbial detectors and a better understanding of the background microbial world in the next decade.

DEFENSE AND COUNTERMEASURES

Vaccines and Medical Countermeasures – Nancy Connell, University of Medicine and Dentistry of New Jersey, USA

Dr. Nancy Connell opened the session by providing an overview of research developments relevant to vaccines and medical countermeasures. Dr. Connell noted that there has been a transition from empirical to rational design of antibiotic and antiviral drugs along with the use of techniques such as combinatorial chemistry. She pointed out that traditional antibiotics targeted nucleic acids and protein and cell wall synthesis, but that newer approaches have targeted additional aspects of virulence such as the production and secretion of toxins. Approaches to modulate host immune functions have also been explored, including stimulation of innate immunity or targeting of the CD45 antigen on macrophages, an antigen shown to be susceptible to attack by some pathogens.

Dr. Connell also discussed developments in vaccines, and again noted that research has moved toward rational design based on increased understanding of the immune system and of host-pathogen interactions. Dr. Connell noted approaches to jump-start components of the immune response such as antigen delivery to dendritic cells to stimulate lymph-node homing and the delivery of engineered MHC Class I single-chain trimers to stimulate T and B cell activation. She pointed out that the first line of exposure to microorganisms is most commonly at mucosal surfaces such as the respiratory and gastrointestinal tracts. As a result, researchers continue to explore ways to generate protective mucosal immunity although challenges remain in understating the biology and interactions with commensal bacteria at these surfaces. Researchers continue to explore new adjuvants as well, to boost the overall immune response or to direct it down cell-mediated or humoral pathways.

Dr. Connell commented on a convergence of multiple technologies with regard to vaccine delivery and future research directions. She highlighted the role of nanotechnology in creating new delivery systems, as well as advances in aerosolization, encapsulation, and techniques such as DNA shuffling. Dr. Connell identified

personalized vaccines, vaccines directed against non-communicable diseases such as cancer and cardiovascular disease, and "lifestyle vaccines" against anything from weight gain to tooth decay as future trends, although it is not yet clear whether all of these will be feasible.

Dr. Connell concluded by noting possible misuses of vaccine and countermeasure knowledge Researchers seek ways to block or reduce the emergence of drug-resistant microbial strains and Dr. Connell commented that some of the knowledge acquired during drug development and testing could potentially be misused, such as information on drug toxicity, drug targets and virulence factors, and drug-resistant strains. Exploration of immune system modulation also raises the possibility of disrupting the balance of biological control systems and affecting interactions among the nervous, endocrine, and immune systems.

Monitoring and Molecular Diagnosis of Emerging Infections – Raymond Lin, National Public Health Laboratory, Singapore

Dr. Raymond Lin spoke to the workshop on monitoring and diagnosis of emerging infections. Dr. Lin emphasized that having an effective public health system to respond to naturally-occurring disease outbreaks also enables preparedness for a biothreat event and noted that a collaborative effort between disciplines such as epidemiology, laboratory microbiology, and clinical practice in responding to new public health concerns is essential.

Dr. Lin discussed several methods of disease monitoring and surveillance–traditional clinical surveillance, seroepidemiology, and predictive modeling–using Singapore's response to H1N1 influenza as an example (Chen et al., 2010; Lee et al., 2010; Ong et al., 2010). Through clinical surveillance, samples were collected daily from sentinel sites among general practitioners and hospitals and combined with laboratory confirmation of influenza and the collection of virus samples for further analysis. These samples were collected not only from symptomatic patients, but from those who were treated for any reason. These data enabled strain typing as well as estimates of the time and number of the population infection peak. In comparison, Singapore tested a serosurvey approach that measured antibodies to influenza. Tested cohorts included military, community, hospitals, and long-term care facilities. Dr. Lin also reported evaluation of a modeling approach, in which symptoms at sentinel clinics were used without confirmatory lab tests. These data generated a range of probabilities for the timing of the population infection peak, with the peak narrowing as more data were collected. The estimates of community infection at the end of September 2009 were compared from the three monitoring

methods, resulting in 5 percent community infection by clinical surveillance, 13 percent by seroconversion data, and 13 percent by predictive modeling. Dr. Lin observed that clinical surveillance with laboratory confirmation can provide relatively real-time information but requires a high volume of testing to achieve accurate statistics. Seroepidemiology is accurate for retrospective infections and can be used to analyze particular subgroups, but can be difficult to organize. Modeling is predictive and easy to organize, but disagreement remains about how useful modeling approaches are to predicting disease and such models need to be verified by other surveillance methods. Countries are also exploring the use of Google search data or social media such as twitter as alternate disease monitoring strategies. So far, however, there is limited data on whether such methods are useful and results may be affected by news-driven peaks (Cook et al., 2010).

Dr. Lin next noted that the 2009 H1N1 outbreak was unprecedented for the speed with which the genomes from viral isolates were sequenced in many countries. He described several ways in which observed or constructed mutations in H1N1 isolates were studied for potential effects on virulence, including D222G in the receptor-binding region and E627K in polymerase basic protein 2, a mutation which had been observed in previous pandemic influenza strains (Maurer-Stroh et al., 2010). However, Dr. Lin noted that study results varied with regard to the effects of these mutations, revealing the limits of our knowledge of the flu. In epidemiology, effective tools for accessing and mining massive amounts of digitized data are needed to draw out significant clusters and alerts. Dr. Lin briefly discussed one such framework, the Care Quest Infection Surveillance and Management (CQ/ISaM) for multi-drug resistant staphylococcus aureus (MRSA), in which clinical data streams are compiled in a central point and can be queried using natural language to generate real-time charts. However, Dr. Lin concluded by emphasizing the important role for front-line physicians to identify outbreaks at the local scale while they remain below the threshold observable through national surveillance systems.

Agricultural Biosecurity: Threats to Crop Production – Michael Jeger, Imperial College London, UK

Dr. Michael Jeger spoke to the workshop about crop security issues. He began by drawing comparisons between traditional and modern methods of crop production, noting that traditional methods often feature small, irregular fields with mixed crops and low use of inorganic fertilizers, herbicides and pesticides, while modern methods feature large, single-crop fields with specially bred cultivars and routine use of chemical products. Dr.

Jeger also noted the extensive biodiversity of plant pathogens, which include viruses, bacteria, fungi, and nematodes.

Dr. Jeger commented that there are several epidemiological scales of disease spread – field level affecting farmers, nationally and regionally affecting national economies, and globally due to both natural and anthropogenic influences. He pointed to the increasing scale of international trade and the potential movement of pathogens through shipping and questioned whether national agricultural health systems are fully prepared to respond to potential outbreaks. He also presented several examples of significant agricultural diseases including the regional and global spread of wheat yellow rust (Brown and Hovmøller, 2002), and noted that devastating banana disease has spread to all of the major growing regions in the world. Dr. Jeger presented data documenting a four-fold increase in identified geminiviruses from 1991-2005 (Rodoni, 2009), and noted that this increase does not appear to be an artifact of increases in sequencing. He highlighted the potentially large economic costs from crop disease outbreaks, suggesting that these diseases may have a major impact whether from accidental or deliberate disease spread.

Dr. Jeger also raised several questions to consider with regard to invasive plant diseases and biosecurity, including the nature of the threat, whether pathogen eradication is feasible, what safeguards should be built into national plant health systems, whether there will be impacts from global trade or climate changes, whether it is possible to predict upcoming concerns, and whether the pathogen that first arrives in a new region or the one that follows is likely to be the most serious problem. With regard to this last point, Dr. Jeger presented a model for how new pathogen strains evolve when introduced into a reservoir (adapted from Antia et al., 2003). He noted that there will be frequent failures of the pathogen to cross over into a new crop species; however a strain will eventually evolve with properties that enable it to emerge as a new pathogen. He also noted that formal plant health regulations may take months or years to be developed, which may not be adequate to respond to accidental or deliberate plant disease outbreaks. Dr. Jeger concluded that improved biosurveillance is needed, along with properly validated methods for collecting and analyzing the information.

Discussion

The discussion following the presentations touched on surveillance systems and ways for the public and agricultural health communities to achieve increased lead time in recognizing emerging disease outbreaks. Among the points noted during the discussion was that current surveillance systems largely rely on passive surveillance, rather than on

the use of active surveillance of sentinel groups. It was also suggested that advances in biotechnology can contribute to the generation of new, pathogen-resistant plant varieties.

COMMUNICATION

How the Internet has Changed Scientific Interchanges – James Meadway, The Royal Society, UK

James Meadway opened the last session with a discussion of the impact of the internet on scientific interchange, pointing out that there has been a significant increase in the amount of information transferred over the internet. To illustrate this point he highlighted how one site, YouTube, now consumes the same bandwidth as the entire internet in 2000. In parallel, there has been a growth in internet access, which although not ubiquitous is becoming increasingly available. Although only a small percentage of the developing world is on the internet, expansion in access in these areas is especially rapid. Advances in physical infrastructure and wireless technology have been complemented by changes in the social infrastructure, and indeed it was suggested that the former enables the latter. While the old World Wide Web "1.0" system was used largely for the replication of mass media technology which was passively consumed, the internet today has become much more interactive and has resulted in the emergence of more user-generated content, much greater depth and complexity of interaction and significant changes in the way people communicate.

This is particularly important for science given that the production of scientific knowledge is fundamentally a social process involving information sharing, collaboration and the mobilization of outputs. The old hierarchy based largely on email enabled instant collaboration and group creation, thus removing some of the barriers to cooperation that previously existed, but also presented limitations for science. New hierarchies like cloud computing have the potential to change the system of collaboration further by making the process of sharing and multi-authoring documents much easier and by placing ideas within a "social" context to allow even more people to contribute.

Dr. Meadway suggested that the development and now potential transformation of the internet may have significant consequences for scientific discovery, including the emergence of new means of conducting research using web 2.0 software, resulting in what some have termed "Science 2.0" (Shneiderman, 2008). The emergence of Science 2.0 through the collaboration and mass dispersal of information eliciting the 'wisdom of crowds' can enable a large number of people to examine the same problem. This process

has the potential to diminish the distinction between formal and informal processes of knowledge creation. The so-called Climate-gate affair illustrates how the release of emails broke down the formal process of knowledge production and allowed the public to enter into the debate.

Dr. Meadway stated that patterns of use differ across disciplines and that we are not quite to Science 2.0 yet. Current developments are largely an extension of existing practices, rather than genuinely new features. Nonetheless, he concluded that it is likely that web 2.0 tools will become more prevalent and there is great potential for a more prevalent science 2.0 approach in the future.

Influence of Technology on Scientific Collaboration – Herawati Sudoyo, Eijkman Institute for Molecular Biology, Indonesia

The second presentation, by Dr. Herawati Sudoyo, addressed the influence of technology on scientific collaboration using the example of disease management in the context of Indonesia. The Indonesian archipelago is the fourth most populous country and experiences serious problems with endemic diseases as well as periodic epidemics, including new emerging diseases. This burden is added to by environmental, ecological and demographic factors spread by travel and trade. As a geographically unique country with a diverse population, Indonesia faces a challenge in managing public health problems, reducing biological risks and promoting capacity building. Due to this diversity, Dr. Sudoyo noted that management of disease is complex and she presented a number of examples of disease challenges including: 15 million cases and 42,000 deaths from malaria in 2005; 529,000 tuberculosis cases in 2007; and 123,174 cases and 1,251 deaths caused by dengue fever in 2007. She noted that hepatitis is particularly problematic, with five sub-genotypes of the virus prevalent in Indonesia as a result of different virus migrations from neighboring countries and regions. As a result, extensive disease surveillance is necessary and has to be supported by the capacity to respond to new emerging infectious diseases.

Dr. Sudoyo detailed how a collaborative partnership of hospitals and research institutions such as the South East Asian Infectious Disease Clinical Research Network (SEAICRN) (Wertheim et al., 2010), had been established and enabled participants in Thailand, Vietnam, and Indonesia to build a multilateral network based on shared principles of respect, sharing and commitment to improve patient management through quality clinical research. The network was intended to build collaboration, cooperation and capacity to tackle disease outbreaks and enabled Indonesia access to state of the art technology and technical training from University of Oxford and its partners. A massive effort to catalog

genetic variation among Asians has also been established with the availability of new technology in the region. She noted that this Pan-Asian SNP Initiative was uniquely conceived by Asians in Asia and executed, funded and completed by an Asian Consortium (The HUGO Pan-Asian NSP Consortium et al., 2009). Japan, Singapore, China and Korea provide technical and scientific training for scientists in less developed countries. In these contexts, internet communication has been particularly useful in sustaining the collaborative process and drawing together 93 researchers from 40 institutions in 11 Asian countries at minimum cost. In the future, a project is planned for the mapping of genetic markers to develop medical countermeasures building on existing Asia-Asia collaboration.

Conveying the Concept of Risk – Terence Taylor, International Council for the Life Sciences

The final speaker in the session, Dr. Terence Taylor, posited that advances in science and technology are the best defense and accordingly noted the need to be cautious when assessing the risks of science to security in order to avoid the demonization of science or the impression that science is dangerous. However, he also emphasized that advances in science raise a number of issues to be considered, including ethics and safety. On this basis, it was suggested that science and technology should be understood along a spectrum of risks with natural risks at one end of the spectrum and deliberate misuse at the other. Moreover, these problems are not limited to any specific country or region, but rather are emerging across the world and pose risks which transcend traditional state boundaries.

Dr. Taylor referred to the work of Robert Carlson on the doubling and proliferation of computational power (Carlson, 2003; Carlson, 2008), and noted that while in 2002 it took 2 years to synthesize polio (Cello et al., 2002), more recently viruses of comparable complexity had been synthesized in only two weeks. The cost of synthesis was also declining at a similar rate. He suggested that it is useful to think about the drivers of S&T, including the information technology (IT) revolution and the diffusion and domestication of IT which propel developments forward, although predicting the future remains extremely difficult. He proceeded to underline the importance of not viewing the biosecurity implications of advances in science as a developed versus developing country issue, and emphasized the importance of implementing a range of actions for dealing with the full spectrum of potential risks. Such actions can include ethics codes and awareness-raising in the life science community, personnel screening, lab security, and building of resilience into systems.

Discussion

The discussion from the last session raised the issue of tacit knowledge and the impact of the internet, with several participants suggesting that the internet allows knowledge to be acquired in a way that would not be possible under other circumstances. There was also further discussion on models and examples of international cooperation. Participants noted the challenges in conducting risk assessments of scientific and technical advances, and the need to both determine the real risks and benefits and to put these into context.

WORKSHOP DISCUSSION SESSIONS AND FINAL REMARKS

In addition to the plenary presentations, the workshop featured two small-group breakout sessions and a final plenary discussion session in which participants were provided with questions that encouraged them to consider the most significant recent and predicted future developments in the areas discussed at the workshop, whether they thought these developments might affect concepts, materials, or delivery mechanisms related to biological weapons, and what technical hurdles could be overcome before there would be cause for concern. Participants were also asked to consider how developments in science and technology could affect biodefense, countermeasures, and mitigation capabilities to address emerging concerns, as well as how future S&T developments might continue to be effectively evaluated in the context of the BWC. The input provided by workshop participants during these sessions informed the discussions of the National Research Council's Committee on Trends in Science and Technology Relevant to the Biological Weapons Convention, and will be incorporated more fully in its forthcoming report.

REFERENCES

Antia, R., R. R. Regoes, J. C. Koella, and C. T. Bergstrom. 2003. The role of evolution in the emergence of infectious diseases. *Nature* 426(6967):658-61.

Brown, J. K. M. and M. S. Hovmøller. 2002. Aerial dispersal of pathogens on the global and continental scales and its impact on plant disease. *Science* 297(5581):537-541.

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

Carlson, R. 2008. Gene synthesis cost update. November 2008; Online. Available at http://www.synthesis.cc/2008/11/; accessed 2/21/2011.

Carlson, R. 2009. The changing economics of DNA synthesis. *Nature Biotechnology* 27:1091-1094.

Cello, J., A. V. Paul, and E. Wimmer. 2002. Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template. *Science* 297(5583):1016–8.

Chalikonda, S., M. H. Kivlen, M. E. O'Malley, X. D. Eric Dong, J. A. McCart, M. C. Gorry, X. Y. Yin, C. K. Brown, H. J. Zeh, 3rd, Z. S. Guo, and D. L. Bartlett. 2008. Oncolytic virotherapy for ovarian carcinomatosis using a replication-selective vaccinia virus armed with a yeast cytosine deaminase gene. *Cancer Gene Therapy* 15:115-125.

Chen, M. I., V. J. Lee, W. Y. Lim, I. G. Barr, R. T. Lin, G. C. Koh, J. Yap, L. Cui, A. R. Cook, K. Laurie, L. W. Tan, B. H. Tan, J. Loh, R. Shaw, C. Durrant, V. T. Chow, A. Kelso, K. S. Chia, and Y. S. Leo. 2010. 2009 influenza A (H1N1) Seroconversion rates and risk factors among distinct adult cohorts in Singapore. *JAMA: the Journal of the American Medical Association* 303(14):1383-1391.

Cohn, M. L., C. L. Davis, and G. Middlebrook. 1958. Airborne immunization against tuberculosis. *Science* 28(3334):1282-1283.

Cook, A. R., M. I. Chen, and R. T. Pin Lin. 2010. Internet search limitations and pandemic influenza, Singapore. *Emerging Infectious Diseases* 16(10):1647-1649.

De Muynck, B., C. Navarre, and M. Boutry. 2010. Production of antibodies in plants: status after twenty years. *Plant Biotechnology Journal* 8:529–563.

Deadwyler, S. A., L. Porrino, J. M. Siegel, and R. E. Hampson. 2007. Systemic and nasal delivery of orexin-A (Hypocretin-1) reduces the effects of sleep deprivation on cognitive performance in nonhuman primates. *Journal of Neuroscience* 27(52):14239-14247.

Dhar, P. K., C. S. Thwin, K. Tun, Y. Tsumoto, S. Maurer-Stroh, F. Eisenhaber, and U. Surana. 2009. Synthesizing non-natural parts from natural genomic template. *Journal of Biological Engineering* 3:2. Available at: http://www.jbioleng.org/content/3/1/2.

Douglas, K. L. 2008. Toward development of artificial viruses for gene therapy: a comparative evaluation of viral and non-viral transfection. *Biotechnology Progress* 24:871-83.

Drmanac, R., A. B. Sparks, M. J. Callow, A. L. Halpern, N. L. Burns, B. G. Kermani, P. Carnevali, I. Nazarenko, G.B. Nilsen, G. Yeung, F. Dahl, A. Fernandez, B. Staker, K. P. Pant, J. Baccash, A. P. Borcherding, A. Brownley, R. Cedeno, L. Chen, D. Chernikoff, A. Cheung, R. Chirita, B. Curson, J. C. Ebert, C. R. Hacker., R. Hartlage, B. Hauser, S. Huang, Y. Jiang, V. Karpinchyk, M. Koenig, C. Kong, T. Landers, C. Le, J. Liu, C. E. McBride, M. Morenzoni, R. E. Morey, K. Mutch, H. Perazich, K. Perry, B. A. Peters, J. Peterson, C. L. Pethiyagoda, K. Pothuraju, C. Richter, A. M. Rosenbaum, S. Roy, J. Shafto, U. Sharanhovich, K. W. Shannon, C. G. Sheppy, M. Sun, J. V. Thakuria, A. Tran, D. Vu, A. W. Zaranek, X. Wu, S. Drmanac, A. R. Oliphant, W. C. Banyai, B. Martin, D. G. Ballinger, G. M. Church, and C. A. Reid. 2010. Human genome sequencing using unchained base reads on self-assembling DNA nanoarrays. *Science* 327(5961):78-81.

Eberwine, J. and T. Bartfai. 2011. Single cell transcriptomics of hypothalamic warm sensitive neurons that control core body temperature and fever response: Signaling asymmetry and an extension of chemical neuroanatomy. *Pharmacology and Therapeutics* 129(3):241-259.

Gibson, D. G., J. I. Glass, C. Lartigue, V. N. Noskov, R. Y. Chuang, M. A. Algire, G. A. Benders, M. G. Montague, L. Ma, M. M. Moodie, C. Merryman, S. Vashee, R. Krishnakumar, N. Assad-Garcia, C. Andrews-Pfannkoch, E. A. Denisova, L. Young, Z. Q. Qi, T. H. Segall-Shapiro, C. H. Calvey, P. P. Parmar, C. A. Hutchison, 3rd, H. O. Smith, and J. C. Venter. 2010. Creation of a bacterial cell controlled by a chemically synthesized genome. *Science* 329(5987):52-56.

Guntur, V. P. and R. Dhand. 2007. Inhaled insulin: extending the horizons of inhalation therapy. *Respiratory Care* 52:911-922.

HUGO Pan-Asian SNP Consortium, M. A. Abdulla, I. Ahmed, A. Assawamakin, J. Bhak, S. K. Brahmachari, G. C. Calacal, A. Chaurasia, C. H. Chen, J. Chen, Y. T. Chen, J. Chu, E. M. Cutiongco-de la Paz, M. C. De Ungria, F. C. Delfin, J. Edo, S. Fuchareon, H. Ghang, T. Gojobori, J. Han, S. F. Ho, B. P. Hoh, W. Huang, H. Inoko, P. Jha, T. A. Jinam, L. Jin, J. Jung, D. Kangwanpong, J. Kampuansai, G. C. Kennedy, P. Khurana, H. L. Kim, K. Kim, S. Kim, W. Y. Kim, K. Kimm, R. Kimura, T. Koike, S. Kulawonganunchai, V. Kumar, P. S. Lai, J. Y. Lee, S. Lee, E. T. Liu, P. P. Majumder, K. K. Mandapati, S. Marzuki, W. Mitchell, M. Mukerji, K. Naritomi, C. Ngamphiw, N. Niikawa, N. Nishida, B. Oh, S. Oh, J. Ohashi, A. Oka, R. Ong, C. D. Padilla, P. Palittapongarnpim, H. B. Perdigon, M. E. Phipps, E. Png, Y. Sakaki, J. M. Salvador, Y. Sandraling, V. Scaria, M. Seielstad, M. R. Sidek, A. Sinha, M. Srikummool, H. Sudoyo, S. Sugano, H. Suryadi, Y. Suzuki, K. A. Tabbada, A. Tan, K. Tokunaga, S. Tongsima, L. P. Villamor, E. Wang, Y. Wang, H. Wang, J. Y. Wu, H. Xiao, S. Xu, J. O. Yang, Y. Y. Shugart, H. S. Yoo, W. Yuan, G. Zhao, B. A. Zilfalil, and Indian Genome Variation Consortium. 2009. Mapping human genetic diversity in Asia. *Science* 326(5959):1541-1545.

Hwang, S. K., J. T. Kwon, S. J. Park, S. H. Chang, E. S. Lee, Y. S. Chung, G. R. Beck, Jr, K. H. Lee, L. Piao, J. Park, and M. H. Cho. 2007. Lentivirus-mediated carboxyl-terminal modulator protein gene transfection via aerosol in lungs of K-ras null mice. *Gene Therapy* 14:1721-1730.

Kim, J and J. Eberwine. 2010. RNA: state memory and mediator of cellular phenotype. *Trends in Cell Biology* 20(6):311-318.

Kosfeld, M., M. Heinrichs, P. J. Zak, U. Fischbacher, and E. Fehr. 2005. Oxytocin increases trust in humans. *Nature* 435(7042):673-676.

Lee, V. J., J. Yap, A. R. Cook, M. I. Chen, J. K. Tay, I. Barr, A. Kelso, B. H. Tan, J. P. Loh, R. Lin, L. Cui, P. M. Kelly, Y. S. Leo, K. S. Chia, W. L. Kang, P. A. Tambyah, and B. Seet. 2010. Effectiveness of public health measures in mitigating pandemic influenza spread: a prospective sero-epidemiological cohort study. *Journal of Infectious Diseases* 202(9):1319-26.

Lipiński, D., J. Jura, R. Kalak, A. Pławski, M. Kala, M. Szalata, M. Jarmuz, A. Korcz, K. Słomska, J. Jura, P. Gronek, Z. Smorag, M. Pieńkowski, R. Słomski. 2003. Transgenic rabbit producing human growth hormone in milk. *Journal of Applied Genetics* 44(2):165-174.

Liu, T. C., E. Galanis, and D. Kirn. 2007. Clinical trial results with oncolytic virotherapy: a century of promise, a decade of progress. *Nature Clinical Practice Oncology* 4(2):101-117.

Luong, J. H., K. B. Male, and J. D. Glennon. 2008. Biosensor technology: technology push versus market pull. *Biotechnology Advances* 26(5):492-500.

Ma, J. K-C., Drake, P. M. W., and P. Christou. 2003. The production of recombinant pharmaceutical proteins in plants. *Nature Reviews Genetics* 4:794-805.

Maurer-Stroh, S., R. T. Lee, F. Eisenhaber, L. Cui, S. P. Phuah, and R. T. Lin. 2010. A new common mutation in the hemagglutinin of the 2009 (H1N1) influenza A virus. *PLoS Currents* (June 1) 2:RRN1162. Available at: http://knol.google.com/k/plos-currents-influenza#.

Medina, M. F., G. P. Kobinger, J. Rux, M. Gasmi, D. J. Looney, P. Bates, J. M. Wilson. 2003. Lentiviral vectors pseudotyped with minimal filovirus envelopes increased gene transfer in murine lung. *Molecular Therapy* 8:777-789.

Mok, H., J. W. Park, and T. G. Park. 2007. Microencapsulation of PEGylated adenovirus within PLGA microspheres for enhanced stability and gene transfection efficiency. *Pharmaceutical Research* 24:2263-2269.

NRC (National Research Council). 2006. *Globalization, Biosecurity, and the Future of the Life Sciences*. Washington, D.C.: The National Academies Press.

NRC. 2009a. *2nd International Forum on Biosecurity: Report of an International Meeting, Budapest, Hungary, March 30-April 2, 2008*. Washington, DC: National Academies Press.

NRC. 2009b. *Strengthening Forensic Science in the United States: A Path Forward*. Washington, D.C.: The National Academies Press.

NRC. 2011a. *Challenges and Opportunities for Education About Dual Use Issues in the Life Sciences*. Washington, DC: National Academies Press.

NRC. 2011b. *Review of the Scientific Approaches Used During the FBI's Investigation of the Anthrax Letters*. Washington, DC: National Academies Press.

Oda, K., Y. Matsuoka, A. Funahashi, and H. Kitano. 2005. A comprehensive pathway map of epidermal growth factor receptor signaling. *Molecular Systems Biology* 1. Available at: http://www.nature.com/msb/journal/v1/n1/full/msb4100014.html and http://systems-biology.org/resources/model-repositories/000272.html.

Ong, J. B., M. I. Chen, A. R. Cook, H. C. Lee, V. J. Lee, R. T. Lin, P. A. Tambyah, and L. G. Goh. 2010. Real-time epidemic monitoring and forecasting of H1N1-2009 using influenza-like illness from general practice and family doctor clinics in Singapore. *PLoS One*. 5(4):e10036. Available at: http://dx.doi.org/10.1371/journal.pone.0010036.

Rodoni, B. 2009. The role of plant biosecurity in preventing and controlling emerging plant virus disease epidemics. *Virus Research* 141(2):150-157.

Roy, C. J. and D. K. Milton. 2004. Airborne transmission of communicable infection- the elusive pathway. *The New England Journal of Medicine* 350(17):1710-1712.

Sepúlveda-Amor, J., J. L. Valdespino-Gómez, Mde L. García-García, J. Bennett, R. Islas-Romero, G. Echaniz-Aviles, and J. F. de Castro. 2002. A randomized trial demonstrating successful boosting responses following simultaneous aerosols of measles and rubella (MR) vaccines in school age children. *Vaccine* 20(21-22):2790-2795.

Shneiderman, B. 2008. "Science 2.0". *Science* 319(5868):1349-1350.

Skrzyszowska, M., Z. Smorag, R. Słomski, L. Katska-Ksiazkiewicz, R. Kalak, E. Michalak, K. Wielgus, J. Lehmann, D. Lipiński, M. Szalata, A. Pławski, M. Samiec, J. Jura, B. Gajda, B. Ryńska, and M. Pieńkowski. 2006. Generation of transgenic rabbits by the novel technique of chimeric somatic cloning. *Biology of Reproduction* 74(6):1114-1120.

Skrzyszowska, M., M. Samiec, R. Słomski, D. Lipiński, and E. Mały. 2008. Development of porcine transgenic nuclear-transferred embryos derived from fibroblast cells transfected by the novel technique of nucleofection or standard lipofection. *Theriogenology* 70(2):248-259.

Sul, J. Y., C. K. Wu, F. Zeng, J. Jochems, M T. Lee, T. K. Kim, T. Peritz, P. Buckley, D. Cappelleri, M. Maronski, M. Kim, V. Kumar, D. Meaney, J. Kim, and J. Eberwine. 2009. Transcriptome transfer produces a predictable cellular phenotype. *Proceedings of the National Academy of Sciences* 106(18):7624-7629.

Suri. S. S., H. Fenniri, B. Singh. 2007. Nanotechnology-based drug delivery systems. *Journal of Occupational Medicine and Technology* 2:16-21.

Tai, B. C., C. Du, S. Gao, A. C. Wan, and J. Y. Ying. 2010. The use of a polyelectrolyte fibrous scaffold to deliver differentiated hMSCs to the liver. *Biomaterials* 31(1):48-57.

Thanavala, Y., Y. F. Yang, P. Lyons, H. S. Mason, and C. Arntzen. 1995. Immunogenicity of transgenic plant-derived hepatitis B surface antigen. *Proceedings of the National Academy of Sciences* 92(8):3358-3361.

Tseng, J., J .L. Komisar, R. N. Trout, , R. E. Hunt, J. Y. Chen, A. J. Johnson, L. Pitt, and D. L. Ruble. 1995. Humoral immunity to aerosolized staphylococcal enterotoxin B (SEB), a superantigen, in monkeys vaccinated with SEB toxoid-containing microspheres. *Infection and Immunity* 63(8):2880-2885.

Venter, J. C. 2010. Multiple personal genomes await. *Nature* 464: 676-677.

Venter, J. C., K. Remington, J. F. Heidelberg, A. L. Halpern, D. Rusch, J. A. Eisen, D. Wu, I. Paulsen, K. E. Nelson, W. Nelson, D. E. Fouts, S. Levy, A. H. Knap, M. W. Lomas, K. Nealson, O. White, J. Peterson, J. Hoffman, R. Parsons, H. Baden-Tillson, C. Pfannkoch, Y. H. Rogers, H. O. Smith. 2004. Environmental genome shotgun sequencing of the Sargasso Sea. *Science* 304(5667):66-74.

Wan, A. C. A., C. U. T. Benjamin, L. Kwong-Joo, and J. Y. Ying. 2006. Silica-incorporated polyelectrolyte-complex fibers as tissue-engineering scaffolds. *Advanced Materials* 18(5)641–644.

Wax, P. M., C. E. Becker, and S. C. Curry. 2003. Unexpected "gas" casualties in Moscow: a medical toxicology perspective. *Annals of Emergency Medicine* 41:700-705.

Wertheim, H. F., P. Puthavathana, N. M. Nghiem, H. R. van Doorn, T. V. Nguyen, H. V. Pham, D. Subekti, S. Harun, S. Malik, J. Robinson, M. Rahman, W. Taylor, N. Lindegardh, S. Wignall, J. J. Farrar, and M. D. de Jong. 2010. Laboratory capacity building in Asia for infectious disease research: Experience from the South East Asia Infectious Disease Clinical Research Network (SEAICRN). *PloS Medicine* 7(4) e1000231. Available at: http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000231

Wolinsky, H. 2007. The thousand-dollar genome. Genetic brinkmanship or personalized medicine? *EMBO Reports* 8(10):900-903.

Zaman, N.T., Y-Y. Yang, and J. Y. Ying. 2010. Stimuli-responsive polymers for the targeted delivery of paclitaxel to hepatocytes. *Nano Today* 5(1):9-14.

APPENDIX

COMMITTEE ON TRENDS IN SCIENCE AND TECHNOLOGY RELEVANT TO THE BIOLOGICAL WEAPONS CONVENTION: AN INTERNATIONAL WORKSHOP

RODERICK J. FLOWER *(Chair)*, Professor of Biochemical Pharmacology, William Harvey Research Institute, Queen Mary University of London, United Kingdom

HERNAN CHAIMOVICH, Superintendent General, Butantan Foundation**,** Professor of Biochemistry, Universidade de São Paulo, Brazil

NANCY D. CONNELL, Professor of Infectious Disease**,** University of Medicine and Dentistry of New Jersey

ANDRZEJ GÓRSKI, Professor of Medicine and Immunology, The Medical University of Warsaw**,** Vice President, Polish Academy of Sciences

LI HUANG, Director-General, Institute of Microbiology**,** Chinese Academy of Sciences

MAXWELL OTIM ONAPA, Deputy Executive Secretary**,** Uganda National Council for Science and Technology

MOHAMED IQBAL PARKER, Professor in Medical Biochemistry, University of Cape Town, South Africa**,** Director, International Centre for Genetic Engineering and Biotechnology, Cape Town

ANDREW PITT, Reader and Director of the Sir Henry Wellcome Functional Genomics Facility, University of Glasgow, Scotland

RALF TRAPP, Consultant, CBW Arms Control and Disarmament**,** France

LLOYD WHITMAN, Deputy Director, Center for Nanoscale Science and Technology**,** U.S. National Institute for Standards and Technology

WORKSHOP RAPPORTEURS

KATHERINE BOWMAN, Senior Program Officer, Board on Life Sciences, U.S. National Research Council

KATHRYN HUGHES, Program Officer, Board on Chemical Sciences and Technology, U.S. National Research Council

JO L. HUSBANDS, Scholar/Senior Project Director, Board on Life Sciences, U.S. National Research Council

JAMES REVILL, Research Fellow, Science Policy Research Unit, University of Sussex, United Kingdom

BENJAMIN RUSEK, Program Officer, Committee on International Security and Arms Control, U.S. National Research Council

WORKSHOP AGENDA

Sunday, 31 October

6:00 PM Reception and Welcome Remarks from Sponsoring Organizations

- *Rod Flower, chair,* Committee on Trends in Science and Technology Relevant to the Biological Weapons Convention: An International Workshop
- *Lei Zhang*, Chinese Academy of Sciences
- *Andrzej Górski*, chair, IAP Biosecurity Working Group
- *Iqbal Parker*, International Union of Biochemistry and Molecular Biology
- *Stephen Lerner*, International Union of Microbiological Societies
- *Meg Flanagan*, Defense Threat Reduction Agency
- *Lorna Miller*, UK Global Partnership Programme
- *Christopher Park*, US Department of State

Monday, 1 November

9:00 AM **Plenary Session 1**: Introduction to the Themes, Goals, and Context of the Workshop
Chair: *Andrzej Górski, Polish Academy of Sciences, Poland*

Welcome Address: *Tao Xu, Director-General, Institute of Biophysics, Chinese Academy of Sciences*

1. Aims and Objectives of the Meeting – *Roderick Flower, Queen Mary University of London, UK*
2. The Biological Weapons Convention: A Brief Overview – *Piers Millet, BWC Implementation Support Unit, United Nations, Switzerland*
3. Introduction to framework for evaluating new science and technology – *Ralf Trapp, CBW Consultant, France*
4. Perspective from the Chinese Academy of Sciences – *Li Huang, Institute of Microbiology, Chinese Academy of Sciences, China*
5. Discussion

10:45 AM **Plenary Session 2**: Developments in Design, Fabrication, and Production (A)
Chair: *Iqbal Parker, University of Cape Town, South Africa*

1. Bioinformatics and Computational Tools – *Etienne de Villiers, International Livestock Research Institute, Kenya*
2. Systems Biology: Relevance to the Biological and Toxins Weapons Convention – *Andrew Pitt, University of Glasgow, UK*
3. Emerging Trends in Synthetic Biology – *Pawan Dhar, University of Kerala, India*
4. Discussion

1:15 PM **Plenary Session 3**: Developments in Design, Fabrication, and Production (B)
Chair: *Andrew Pitt, University of Glasgow, UK*

1. Bioreactors and Transgenic Animals – *Ryszard Słomski, Poznań University of Life Sciences, Poland*

2. Transgenic Plants and Recombinant Pharmaceuticals – *Julian Ma, St. Georges University of London, UK*
3. Neuroscience Developments – *James Eberwine, University of Pennsylvania School of Medicine, USA*
4. Discussion

3:00 PM **Plenary Session 4**: Dispersal and Delivery
Chair: *Ralf Trapp, CBW Consultant, France*

1. Aerosols and Aerobiology – *Chad Roy, Tulane National Primate Research Center, USA*
2. Nanostructured Delivery Systems for Drugs, Proteins and Cells – *Jackie Ying, Institute of Bioengineering and Nanotechnology, Singapore*
3. Commentary: Implications Stemming From Advances in Dual-Use Targeted Delivery Systems – *Kathryn Nixdorff, Darmstadt University of Science and Technology, Germany*
4. Discussion

4:15 PM **Breakout Discussion Sessions**

7:30 PM **Special Event**: "Strengthening the culture of responsibility with respect to dual use research and biosecurity" (videoteleconference). Organized by NIH/NSABB and the Chinese Academy of Sciences, in cooperation with the IAP, IUMS, IUBMB, and NAS

Tuesday, 2 November

9:00 AM **Plenary Session 5**: Summary from Day 1
Chair: *Maxwell Otim Onapa, Uganda National Council for Science and Technology, Uganda*

1. Presentations from Rapporteurs of Day 1 Breakout Sessions
2. Discussion

9:30 AM **Plenary Session 6:** Detection, Identification, and Monitoring
Chair: *Lloyd Whitman, National Institute of Standards and Technology, USA*

1. Postgenomic Technologies – *Andrew Pitt, University of Glasgow, UK*
2. Exploring an International Microbial Forensics Capability to Support Attribution and Advance Global Biosecurity – *Randall Murch, Virginia Polytechnic Institute and State University, USA*
3. Biosensors Overview – *Gary Resnick, Los Alamos National Laboratory, USA*
4. Biosensor Development – *Ilya Kurochkin, M.V. Lomonosov Moscow State University, Russia*
5. Remarks: Brief Summary of the Science used by the FBI in the Anthrax Attacks Case of 2001 - *Nancy Connell, University of Medicine and Dentistry of New Jersey, USA*
6. Discussion

11:15 AM **Plenary Session 7**: Defense and Countermeasures
Chair: *Anwar Nasim, COMSTECH, Pakistan*

1. Vaccines and Medical Countermeasures – *Nancy Connell, University of Medicine and Dentistry of New Jersey, USA*
2. Monitoring and Molecular Diagnosis of Emerging Infectious Diseases – *Raymond Lin, National Public Health Laboratory, Singapore*
3. Agricultural Biosecurity: Threats to Crop Production – *Michael Jeger, Imperial College London, UK*
4. Discussion

1:45 PM **Breakout Discussion Sessions**

4:15 PM **Plenary Session 8**: Communication
Chair: *Hernan Chaimovich, Fundação Butantan, Brazil*

1. How the Internet has Changed Scientific Interchanges – *James Meadway, The Royal Society, UK*
2. Influence of Technology on Scientific Collaboration: Indonesia Experience – *Herawati Sudoyo, Eijkman Institute for Molecular Biology, Indonesia*
3. Biological Risks – Future Trends: Conveying the Concept of Risk – *Terence Taylor, International Council for the Life Sciences, USA*
4. Discussion

Wednesday, November 3

9:00 AM **Plenary session 9**: Summary from Day 2
Chair: *Li Huang, Institute of Microbiology, Chinese Academy of Sciences, China*

1. Presentations from Rapporteurs of Day 2 Breakout Sessions
2. Discussion of Days 1 and 2

10:30 AM **Plenary session 10**: Workshop Conclusions
Chair: *Roderick Flower, Queen Mary University of London, UK*

1. Facilitated Discussion: Improving Scientific Input into the BWC
2. Discussion of Workshop Findings and Conclusions
3. Next Steps

12:00 PM Meeting Adjournment

PARTICIPANT LIST

Katherine Bowman
Board on Life Sciences
The U.S. National Academies

Göran Bucht
Swedish Defense Research Establishment

Hernan Chaimovich
Fundação Butantan
University of São Paulo

Teck-Mean Chua
Asia Pacific Biosafety Association

Nancy Connell
Department of Medicine
University of Medicine and Dentistry of New Jersey

Neil Davison
Security and Diplomacy
The Royal Society

Etienne De Villiers
International Livestock Research Institute

Pawan Dhar
Centre for Systems and Synthetic Biology
University of Kerala

Gang Dong
Chinese Academy of Military Medical Sciences

Qi Dong
Division of International Organization
Bureau of International Cooperation
Chinese Academy of Sciences

Cris dos Remedios
International Union for Pure & Applied Biophysics
University of Sydney

James Eberwine
Department of Pharmacology
University of Pennsylvania School of Medicine

Gerald Epstein
Center for Science, Technology, and Security Policy
American Association for the Advancement of Science

Meg Flanagan
U.S. Defense Threat Reduction Agency

Rod Flower
St. Barts and The London School of Medicine
Queen Mary University of London

David R. Franz
Midwest Research Institute

David Friedman
Institute for National Security Studies
Tel-Aviv University

Katsuhisa Furukawa
Japan Science and Technology Agency

Andrzej Gorski
Polish Academy of Sciences

Anfeng Guo
Visiting Fellow, Princeton University
Beijing Science Technology and Security Center

Li Huang
Institute of Microbiology
Chinese Academy of Sciences

Kathryn Hughes
Board on Chemical Sciences and Technology
The U.S. National Academies

Jo L.Husbands
Board on Life Sciences
The U.S. National Academies

Saied Jaradat
Princess Haya Biotechnology Center

Michael J. Jeger
Imperial College London

Serhiy Komisarenko
National Biosafety and Biosecurity Commission
Academy of Sciences of Ukraine

Gabriele Kraatz-Wadsack
Weapons of Mass Destruction Branch
Office for Disarmament Affairs

Ilya Kurochkin
Chemical Department
M.V. Lomonosov Moscow State University

Valdas Laurinavicius
Institute of Biochemistry
Vilnius University

Stephen Lerner
International Union of Microbiological Societies
Wayne State University School of Medicine

Ming Li
Beijing Institutes of Biological Science
Chinese Academy of Sciences

Zhenjun Li
Department of Science & Education
National Institute for Communicable Disease Control and Prevention
China CDC

Raymond Lin
National Public Health Laboratory
Ministry of Health

Shu Liu
Chinese Academy of Military Medical Sciences

Yidong Liu
Institute for the History of Natural Science
Chinese Academy of Sciences

Julian Ma
St George's Hospital Medical School
University of London

Irma Makalinao
Department of Pharmacology and Toxicology, College of Medicine
University of the Philippines Manila

Robert Mathews
NBC Arms Control Unit
Defence Science and Technology Organisation

James Meadway
The Royal Society

Sue Meek
Australian Academy of Science

Lorna Miller
Defence Science and Technology Laboratory

Piers Millett
BWC Implementation Support Unit
United Nations

Randall Murch
Virginia Polytechnic Institute and State University

Anwar Nasim
OIC Standing Committee on Scientific and Technological Cooperation (COMSTECH)

Kathryn Nixdorff
Darmstadt University of Technology

Godwin Haruna Ogbadu
Sheda Science and Technology Complex

Maxwell Otim Onapa
Uganda National Council for Science and Technology

Christopher Park
Bureau of International Security and Nonproliferation
U.S. Department of State

M. Iqbal Parker
International Centre for Genetic Engineering and Biotechnology
University of Cape Town

Graham Pearson
Department of Peace Studies
University of Bradford

Lei Pei
Organisation for International Dialogue & Conflict Management

Andrew Pitt
University of Glasgow

Yerlan Ramankulov
National Center for Biotechnology of the Republic of Kazakhstan

I. Gary Resnick
Bioscience Division
Los Alamos National Laboratory

James Revill
Science and Technology Policy Research
University of Sussex

Chad Roy
Tulane National Primate Research Center
Tulane University School of Medicine

Benjamin Rusek
Committee on International Security and Arms Control
The U.S. National Academies

Nariyoshi Shinomiya
Department of Integrative Physiology and Bio-Nano Medicine
National Defense Medical College of Japan

Aleksandr Simonian
Biosensing/CBET
National Science Foundation

Ryszard Slomski
Department of Biochemistry and Biotechnology
Poznan University of Life Sciences

James Stack
Kansas State University
Great Plains Diagnostic Network

Colonel Ben Steyn
Chemical and Biological Defence Advisor
South African Military Health Service

Herawati Sudoyo
Eijkman Institute for Molecular Biology

Leiv Sydnes
Department of Chemistry
University of Bergen

Marlena Szalata
Department of Biochemistry and Biotechnology
Poznan University of Life Sciences

Terence Taylor
International Council for the Life Sciences

Ralf Trapp
Consultant, CBW Arms Control and Disarmament

Jinglin Wang
Institute of Microbiology and Epidemiology
Chinese Academy of Military Medical Sciences

Lei Wang
Chinese Academy of Military Medical Sciences

Li Wang
Chinese Academy of Military Medical Sciences

Lloyd Whitman
Center for Nanoscale Science and Technology
National Institute for Standards and Technology (NIST)

Angela Woodward
Verification Research, Training and Information Centre (VERTIC)

Jackie Ying
Institute of Bioengineering and Nanotechnology

Zhiming Yuan
Wuhan Institute of Virology
Chinese Academy of Sciences

Lei Zhang
Institute of Biophysics
Chinese Academy of Sciences

Xiushan Zhang
Chinese Academy of Military Medical Sciences

Lianhui Zhu
Chinese Academy of Military Medical Sciences

Enlin Zhu
Plant Protection and Plant Quarantine Division
Ministry of Agriculture