National Institutes of Health
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Office of Biotechnology Activities

NATIONAL SCIENCE ADVISORY BOARD FOR BIOSECURITY

March 30, 2006
National Institutes of Health Campus
9000 Rockville Pike
Building 31, 6C Room 10
Bethesda, MD

MEETING SUMMARY

VOTING MEMBERS

Dennis L. Kasper, M.D., NSABB Chair
Arturo Casadevall, M.D., Ph.D.
Murray L. Cohen, Ph.D., M.P.H., C.I.H.
Susan A. Ehrlich, J.D.
Lynn Enquist, Ph.D.
Barry J. Erlick, Ph.D.
David R. Franz, D.V.M., Ph.D.
Michael J. Imperiale, Ph.D.
Paul S. Keim, Ph.D.
Stanley M. Lemon, M.D.
Stuart B. Levy, M.D.
John R. Lumpkin, M.D., M.P.H.
Mark E. Nance, J.D.
Michael T. Osterholm, Ph.D., M.P.H.
David A. Relman, M.D.
James A. Roth, D.V.M., Ph.D.
Harvey Rubin, M.D., Ph.D.
Admiral William O. Studeman (Ret.)
Anne K. Vidaver, Ph.D.
Diane W. Wara, M.D.

EX OFFICIO MEMBERS

Jason E. Boehm, Ph.D.
Brenda A. Cuccherini, Ph.D., M.P.H.
Anthony S. Fauci, M.D.
Elizabeth George, Ph.D.
Sue Haseltine, Ph.D.
Maryanna Henkart
Peter R. Jutro, Ph.D.
Dale Klein, Ph.D.
Terry Lomax, Ph.D.
Boris D. Lushniak, M.D., M.P.H.
Claudia A. McMurray, J.D.
Janet K. A. Nicholson, Ph.D.
Stuart L. Nightingale, M.D.
Caird E. Rexroad, Jr., Ph.D.
Scott Steele, Ph.D.
David G. Thomassen, Ph.D.
Vincent L. Vilker, Ph.D.
Ronald Walters, Ph.D.

NATIONAL INSTITUTES OF HEALTH REPRESENTATIVES

Amy Patterson, M.D., Acting NSABB Executive Director

GUEST SPEAKERS

David Carr
Strategic Planning and Policy Unit, Wellcome Trust

Ottorino Cosivi, D.V.M.
Department of Epidemic and Pandemic Alert and Response, World Health Organization

Barry Kellman, J.D.
International Human Rights Law Institute, DePaul University

Terrence Taylor
International Council for the Life Sciences

CALL TO ORDER
Dennis L. Kasper, MD
Amy Patterson, MD

Dr. Kasper called to order the fourth meeting of the National Science Advisory Board for Biosecurity (NSABB) at 8:15 a.m. He introduced himself and welcomed the Board members as well as members of the public who were in attendance and those watching via web cast. Introductions were made around the table. Dr. Kasper noted that NSABB members Andrew Sorensen, Adel Mahmoud, Claire Fraser, Thomas Shenk, and John Gordon could not be present. Ex officio members also introduced themselves.

Dr. Patterson read aloud the Government regulations concerning conflicts of interest, reminding members that they are required to recuse themselves in advance of any discussion in which they perceive a conflict of interest.

Dr. Kasper referred to the copy of the November 2005 NSABB meeting minutes distributed in advance of the meeting and called for a motion to approve them. It was so moved and seconded, and the minutes were unanimously approved.

INTRODUCTION AND AGENDA OVERVIEW
Dennis L. Kasper, MD

Dr. Kasper explained that the purpose of the NSABB is to provide advice, guidance, and leadership regarding biosecurity oversight of dual use research, that is, life sciences research that has the potential to be misused to threaten public health and other aspects of national security. He noted that the NSABB has been charged with a number of specific tasks and that the Board has formed working groups to address them:

- Criteria for identifying dual use research
- Tools for the responsible communication of dual use research
- Synthetic Genomics
- International collaboration for the oversight of dual use research
- Codes of Conduct

The work of each of these groups, said Dr. Kasper, is part and parcel of developing a framework for the oversight of dual use research.

DUAL USE CRITERIA WORKING GROUP: STATUS REPORT
Dennis L. Kasper, M.D.

Dr. Kasper began by noting that one of the specific tasks of the NSABB is to develop a set of criteria to identify dual use research and research results. To that end, the Criteria Working Group was established at the NSABB inaugural meeting and has been developing a set of draft criteria for the full board's consideration. Stressing that the criteria were being presented as a

working draft and still subject to revision, Dr. Kasper invited feedback from both the Board and the community at large on the work of the group.

Dr. Kasper noted that throughout their deliberations, the working group members were concerned about preventing or reducing the likelihood of misapplication of bioresearch without hindering the efforts of researchers. The working group wanted to focus the criteria on specific types of research with results that would be of greatest concern in terms of the potential for harmful consequences if misused. As a result, they decided the wording "dual use research *of concern*," was more appropriate than "dual use research." The designation of "research of concern," explained Dr. Kasper, does not indicate *a priori* that the research should not be performed, or that the results should not be published, but instead that the research may warrant special consideration and oversight during its conduct and communication.

The working group began its task by considering various factors that might be used to delineate dual use research of concern. From these deliberations, the following key concepts emerged:

1. The primary goal of identifying dual use research of concern is to minimize the potential for misuse of biotechnology without hindering the progress of science and the important benefits that it yields.

2. Any biosecurity concerns pertaining to the misapplication of information or technologies resulting from research should be considered independently from biosafety concerns.

3. Because life sciences research is an extraordinarily dynamic field that encompasses many diverse disciplines, it will be necessary to periodically review the criteria for identification of dual use research of concern and to modify these as necessary to ensure they are relevant and reflect new advances and technologies.

4. There is a compelling need for the criteria to be sufficiently specific to ensure they capture only that research which is dual use of concern.

5. Any successful dual use research management strategy will require effective identification, evaluation, and oversight of dual use research at the local level. As such, the principal investigator (PI) and the research institution should be primarily responsible for accomplishing this.

Dr. Kasper then presented the working group's basic working draft for identifying dual use research of concern (see box "Working Draft of the Criteria," below).

Working Draft of the Criteria

It is likely that the knowledge, products, or technologies derived from this research could be inadvertently or deliberately misapplied by others to pose a threat to public health, agriculture, plants, animals, the environment, or materiel. Of particular concern is research that is likely to (any of the following):

a. Render an immunization ineffective or disrupt immunity
b. Confer to a pathogenic agent or toxin resistance to clinically and/or agriculturally useful prophylaxes or therapeutics against that agent or toxin
c. Enhance the pathologic consequences of an agent or toxin
d. Increase the transmissibility of a pathogenic agent
e. Increase the capability of a pathogenic agent or toxin to be disseminated
f. Alter the host range or tropism of a pathogenic agent or toxin
g. Enhance the susceptibility of a host population
h. Generate a novel pathogenic agent or toxin or reconstitute an eradicated pathogenic agent

Dr. Kasper also referred the board members to a check sheet in their binders that the working group proposes for use by individual investigators to identify dual use research of concern (see box "Worksheet for Dual Use Potential," below).

Worksheet for Dual Use Potential

Question 1: Is it likely that the research could enable the:

a. Rendering of an immunization ineffective or disruption of immunity?
b. Confirmation [*sic*] to a pathogenic agent or toxin resistance to clinically and/or agriculturally useful prophylaxes or therapeutics against that agent or toxin?
c. Enhancement of the pathologic consequences of an agent or toxin?
d. Increase in transmissibility of a pathogenic agent?
e. Increase in the capability of a pathogenic agent or toxin to be disseminated?
f. Alteration of the host range or tropism of a pathogenic agent or toxin?
g. Enhancement of the susceptibility of a host population?
h. Generation of a novel pathogenic agent or toxin or the reconstitution of an eradicated pathogenic agent?

Question 2: Criteria for identifying Dual Use Research of Concern: Including considerations of Question 1a–h above, is it likely that the knowledge, products, or technologies derived from this research could be inadvertently or deliberately misapplied by others to pose a threat to public health, agriculture, plants, animals, the environment, or materiel?

Question 3: Does the research involve a select agent or an agent that requires BSL-4 containment?

To ensure that the criteria focuses primarily on research that may produce results of greatest concern, the working group began by circumscribing those areas of the life sciences that pose the greatest potential for harm. The group examined the existing literature, including the National Research Council's reports *Globalization, Biosecurity, and the Future of the Life Sciences*[1] and *Biotechnology Research in an Age of Terrorism*.[2] In the course of identifying the specific areas of concern, the working group recognized that it was necessary to achieve a practical balance and that the criteria must provide unambiguous guidance without being inflexible or overly prescriptive. The working group strove to identify and refine particular research areas of concern with the objective of providing a clear and concise guide for evaluating research for its dual use potential.

Dr. Kasper next presented each of the research areas of concern outlined in the draft criteria (a-h), along with the working group's rationale for inclusion. He emphasized that only research posing a threat to "public health, agriculture, plants, animals, the environment, or materiel" should be considered dual use research of concern.

a. Render an immunization ineffective or disrupt immunity:

This type of research could allow a host population to become susceptible to a disease that it would otherwise have been protected against. The term *immunization* refers to the active or passive induction of immunity through inoculation or infection, including antitoxins and toxoids. The term *immunity* encompasses all aspects of host immunity, both adaptive and innate.

b. Confer to a pathogenic agent or toxin resistance to clinically and/or agriculturally useful prophylaxes or therapeutics against that agent or toxin:

The inability to effectively prevent or treat various diseases caused by certain pathogenic agents or toxins can result in significant economic and logistical burdens to the public health infrastructure, compromise the food supply, and cause other related adverse consequences. The term *pathogenic agents* includes infectious vectors capable of causing a pathologic change in the host. *Clinically and/or agriculturally useful prophylaxes or therapeutics* include first- or second-line treatment measures or alternative treatment measures for special populations, such as pregnant women or immunologically compromised individuals.

c. Enhance the pathologic consequences of an agent or toxin:

The ability to treat a disease may be compromised if prophylaxes or therapeutics are no longer effective. *Pathogenic consequences* refers to properties such as virulence, infectivity, toxicity, and the route of exposure to a toxin.

d. Increase the transmissibility of a pathogenic agent:

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[1] Institute of Medicine, National Research Council. *Globalization, Biosecurity, and the Future of the Life Sciences.* Washington, DC: National Academies Press, 2006. Executive Summary available at http://fermat.nap.edu/catalog/11567.html. Retrieved May 11, 2006.

[2] National Research Council. *Biotechnology Research in an Age of Terrorism.* Washington, DC: National Academies Press, 2004. Available at http://fermat.nap.edu/books/0309089778/html. Retrieved May 11, 2006.

Increasing the rate or ease with which a pathogenic agent can spread could impede attempts to treat disease and contain disease outbreaks. *Transmissibility* refers to the ease with which an agent spreads from the host, or the contagiousness of an organism, as well as its infectivity. This includes transmission between hosts of the same species or between hosts of differing species.

e. Increase the capability of a pathogenic agent or toxin to be disseminated:

Effective dissemination of a pathogenic agent or toxin could result in large-scale exposure and the inability to prevent or treat ensuing disease and/or damage. The term *dissemination* in this element of the criteria refers to the ability to effectively spread an agent or toxin among a host population, the environment, or materiel so as to ensure significant exposure. The working group differentiated *dissemination* here from its use in the previous element (d), which refers to transmissibility. In this element, the term refers to the population base, including the environmental stability, for example, of an agent or toxin.

Dr. Kasper noted that there are inherent difficulties involving magnitude and intent embedded in this area of concern. Dr. Kasper also noted that this area of research should receive particular attention when guidelines are developed.

f. Alter the host range or tropism of a pathogenic agent or toxin:

Altering the host range of a pathogenic agent or toxin would endanger populations that would not normally be susceptible and for which prophylaxes and therapeutics may not be available. *Host range* refers to the number of different species that can become infected by a pathogen, causing disease in the host or causing it to become a carrier.

g. Alter the susceptibility of a host population:

Rendering a host population vulnerable to the pathogenic consequences of an agent or toxin could result in disease outbreaks of epidemic proportions. This area of concern is not intended to include research involving an individual or a cohort, but rather a population. The term *population* implies that information yielded by such research could be misapplied for large-scale effects.

h. Generate a novel pathogenic agent or toxin, or reconstitute an eradicated pathogenic agent:

This element applies to agents and toxins for which there is no known or widely available prophylaxis or therapeutic, as well as agents that could evade diagnostics and for which there is little known immunity. A novel agent or toxin is one that is not known to have previously existed in nature and is considered unique on the basis of biologic or other properties. Eradicated agents include those thought to no longer exist or those thought to not be in circulation.
Dr. Kasper explained that the working group considered other elements but did not include them in the draft criteria. Among these were "weaponization" and "evasion of diagnostic and detection modalities," which the group felt were encompassed in the wording of the areas of concern; therefore, there was no need to introduce terms that may add ambiguity. The group also excluded

equipment because of the difficulty in identifying a category(ies) of equipment used in life sciences research that would cause research to be classified as "dual use of concern" by virtue of its use.

Although the Criteria Working Group was not charged with developing guidelines for the oversight of dual use research, some evaluation and oversight issues arose during the group's development of the draft criteria. The working group conceptualized a process for the identification and oversight of dual use research and a general process for facilitating a focused review of those criteria. This process would encompass four levels of review:

1. An **initial assessment**, which would determine whether the research should be considered "dual use of concern." This assessment would be the responsibility of the PI, who would use the worksheet developed by the working group.

2. If the research is determined to be dual use research of concern, an **institutional review** by a "designated knowledgeable institutional official or committee" (to be identified) would be conducted to determine whether additional oversight is needed.

3. **Institutional guidance and oversight** would ensure that institutional responsibilities are being met (e.g., for reviews and assessments) and would coordinate and monitor oversight of the research.

4. **Federal guidance and oversight** would ensure compliance and would periodically allow for reevaluation and updating of the criteria.

The working group tested the worksheet for dual use potential using various research scenarios. Dr. Kasper noted that this exercise proved to be extremely useful and presented example cases used by the group as they tested the worksheet.

For next steps, Dr. Kasper invited feedback from the NSABB on the working draft of the criteria. With NSABB's approval, the working group would like to solicit broader public feedback and input.

Discussion

Dr. Lemon expressed concern over the inclusion of Question 3 on the Worksheet for Dual Use Potential ("Does the research involve a Select Agent or an agent that requires BSL-4 containment?"). He noted that a rigid process to ensure the security of Biosafety Level (BSL)-3 and BSL-4 agents is already in place. In addition, he speculated that the inclusion of this criterion might convey the impression that the term "dual use" applies only to BSL-4 agents. He also noted that many BSL-3 organisms are equally as dangerous as BSL-4 agents. Although, as Dr. Lemon pointed out, the physical containment and biosecurity of these agents are addressed through the existing Select Agent Act and the USA PATRIOT (Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism) Act, there is no current guidance regarding their use in research. Dr. Kasper and Dr. Imperiale, who is also on the Criteria Working Group, noted that the question regarding BSL-4 agents is not a part

of the criteria for dual use research of concern, but rather is intended to prompt a biosecurity review for experiments involving these agents. Later in the discussion, Dr. Franz echoed Dr. Lemon's concerns about Question 3 and stated that he would attempt to draft some language that would better address the concerns, to be shared with the working group online.

Dr. Enquist asked whether the working group considered including elements to address certain types of technology that might be diverted for nefarious purposes. He referred specifically to a method of disrupting the immune response to adenoviruses and adeno-associated viruses to prevent interference with second or third immunization or treatment with gene therapy vectors by introducing viral capsids that do not bind to neutralizing antibodies. This method was reported in a prominent journal. Dr. Kasper replied that the working group discussed technology at length in formulating the criteria but ultimately decided, for practical purposes, to define the results of the research rather than the mechanism used to achieve that result.

An unidentified audience member asked who would use the questionnaire developed by the working group, that is, whether it would be used for all National Institutes of Health (NIH) submissions or only a subset of applications for research directed at microbiotechnology. Dr. Kasper explained that the details are forthcoming, but agreed that researchers using microbes would probably use the worksheet. He asked the Board members for their thoughts on this question. Dr. Keim, who is the chair of the Communications Working Group, said that his group has developed a similar tool and has discussed this issue. The members of that group feel that one of the most common uses for such a tool would be in an educational setting, perhaps as part of an ethics training program. Dr. Kasper agreed that education and training would be important uses for the instrument.

Dr. Rubin asked whether the Criteria Working Group had given any thought to developing guidelines specifically for Question 2 on the worksheet, since this element refers to "other individuals" over whom the researcher has no control. Dr. Kasper agreed that risk management is a significant issue and will be considered during the development of guidelines, which is the next step in the establishment of an oversight process for dual use research of concern. He said that this issue prompted the concept of designating a second institutional individual (the "designated knowledgeable institutional official" referred to in the second level of review) to conduct a secondary review of research that is potentially identified as dual use of concern.

Dr. Franz asked how the working group proposed to address drug discovery programs which deal with the artificial production of natural toxins created by animals, plants, or microbes. Dr. Erlick, a member of the Criteria working group, stated that the group decided not to address the area of biochemical synthesis.

Dr. Casadevall observed that the wording of Question 2, "Is it likely...?" calls for a judgment, and points to the need for education and training to accompany use of the questionnaire. He noted that this wording provides some latitude for the reasoned exercise of the user's judgment without hindering the review process by unnecessary scrutiny of research that is clearly beneficial, such as cancer and vaccine research. Dr. Kasper agreed, noting that the group consciously chose this wording in order to set the bar high enough to exclude extremely unlikely scenarios. Other Board members agreed that this wording was appropriate and useful.

Dr. Keim noted that the need to educate more than 400 Institutional Biosafety Committees (IBCs) in the United States (at a later point in the meeting, Dr. Patterson corrected this figure to more than 600 IBCs) regarding the use of the criteria worksheet presents a daunting task in order to identify what will probably be an infrequent occurrence. In the Communications Working Group, one idea that was discussed was for a more regional type of approach whereby specialized committees are developed at a higher level than the university and institutional levels. It was suggested that the Regional Centers of Excellence (RCEs) sponsored by NIH might be an effective mechanism for the establishment of these types of dual use oversight committees. This would entail the use of fewer people and a more streamlined process. Rhona Hirschberg, one of the program officers for the RCE program at the NIH National Institute of Allergy and Infectious Diseases, agreed that this was an interesting possibility and worth considering. Later in the discussion, Dr. Imperiale commented that an advantage of keeping oversight at the institutional level is the assurance of having the appropriate type and level of expertise. Another advantage is the ease with which review can be expedited when necessary. Dr. Keim said that the volume of reviews would be one factor driving whether a regional or an institutional level of review would be more beneficial. To avoid a bureaucratic morass, Dr. Levy suggested the review process be kept at the institutional level, while the RCEs are used for educational and training purposes. Dr. Keim agreed that another model would be to have a regional or even national committee to serve as a resource for the RCEs. Dr. Vidaver suggested that a body akin to the NIH Recombinant DNA Advisory Committee might be established to conduct the reviews at the regional level.

Judge Ehrlich suggested that the concept of public safety be added to that of public health, because public safety denotes a level of physical security that is independent of health. She explained that threats to public safety might be commercial or economic and would have widespread incidental and indirect effects. Dr. Casadevall stated that many of these concerns should be covered under the concept of "materiel" that is already incorporated into the criteria.

Dr. Cohen noted that training would be needed for consistent application of the criteria and is likely to be a formidable undertaking. He questioned whether some industry other than biomedical research, such as law enforcement or exporting, might already have developed some of the same concepts, guidelines, and criteria that could be usefully applied to dual use research. Dr. Imperiale pointed out that training would still be needed, should this be the case.

Dr. Lemon commented that it is difficult to establish criteria without knowing the consequences for research that meets these criteria or the nature of the subsequent biosecurity review. He advised that the criteria should remain in draft form until the entire process can be laid out. Dr. Kasper agreed, stating that the working group's intentions at this time are to inform the remainder of the Board of their deliberations and to obtain feedback.

Dr. Rubin asked whether the research described in a report in the *Proceedings of the National Academy of Sciences* outlining vulnerabilities that could be used to orchestrate a potential

bioterror attack on the U.S. milk supply[3] would be considered to fall under element "e" of the draft criteria. In response, Dr. Erlick stated that this scenario described a mechanism for dissemination and that the group wished to confine the issue specifically to research. He suggested that issues raised by this manuscript might be better fielded by the Communication Working Group. Dr. Osterholm, who is a member of the Criteria Working Group, said that the scenarios outlined in the same article were not the type that a researcher working with botulinum toxin would be likely or expected to anticipate.

Dr. Kasper briefly and informally surveyed Board members on the number of applications they receive at their institutions that potentially fit the draft criteria. The answers ranged from several per month to 10 per year.

Dr. Cohen pointed out that the terms *biosafety* and *biosecurity* are used and defined differently by various U.S. Government agencies and international organizations. He encouraged the group to cross-reference the definitions used in the criteria with those that are being wordsmithed in anticipation of the upcoming Biological Weapons Convention review. Dr. Cohen offered to pass along to the workgroup the current definitions in the draft fifth edition of the BMBL, as well as revisions in the WHO's third edition of its Laboratory Biosafety Manual.

Dr. Avital Bar-Shalom of the U.S. House of Representatives Committee on Science expressed concern that the working group decided to omit and the term "weaponization" in the draft criteria. Dr. Kasper stated that the group based this decision on the difficulties encountered in defining boundaries in specific applications, such as the area of diagnostics. Dr. Relman concurred and stated that future discussions might encompass the area of diagnostics, particularly those related to critical vulnerabilities associated with an unusual approach or basis for detection and diagnosis. Dr. Erlick stated that the working group even struggled with the term *weaponization* and that any method of increasing pathogenicity could conceivably be considered a potential part of a weaponization process. He said that the term is not clearly defined because it is a process. The group indicated that they will continue to consider these, as well as other areas, for inclusion as this is a draft version of these criteria.

CODE OF CONDUCT WORKING GROUP: STATUS REPORT
Mark Nance, J.D.

Mr. Nance reported that the Codes of Conduct Working Group has identified a number of key concepts: 1) that codes of conduct are distinct from procedural guidelines because they provide general guideposts for responsible and ethical behavior in contrast to prescriptive standards; 2) that codes can be useful in promoting a culture of responsibility, which is one of the primary objectives of the NSABB; 3) that codes can be international in scope; and 4) that there is a critical need to invite the research community to provide appropriate feedback during the process of recommending a code, which should also facilitate the adoption of a code once it is promulgated.

[3] Wein LM, Liu Y. Analyzing a bioterror attack on the food supply: the case of botulinum toxin in milk. Proc Natl Acad Sci U S A. 2005;102(28):9984–9989. E-publication ahead of print, 2005 Jun 28. Available at http://www.pnas.org/cgi/content/full/102/28/9984. Retrieved May 12, 2006.

As background to its work, the working group surveyed existing codes to identify common values and standards and to isolate those elements that are of greatest relevance to the issues associated with dual use research and biosecurity in general. The group then considered the target audience for the code, as well as the value of contextual information, such as the concerns associated with dual use research, the value of education in preventing the misuse of research, and how the code will be used.

The working group proposed that the code of conduct have three major sections: 1) a preamble providing an introductory overview of dual use research and describing the utility of codes, 2) core guiding principles stating the fundamental tenets of responsible behavior, and 3) the body of the code itself. Mr. Nance outlined the major principles that the group has identified to date, which include awareness about dual use research, forethought in the planning and conduct of research, and consideration for the safety and security of others.

The working group has conducted focus groups to provide feedback for the further refinement of a draft code. Participants in these focus groups have included practicing scientists, administrators, leaders in scientific and professional organizations, institutional oversight personnel, and ethicists. Questions and answers were targeted toward the types of participants involved, as well as general attitudes about codes and dual use research. Most participants had prior experience with codes and were positive about their impact. Opinions varied in terms of the effectiveness of codes in influencing behavior, noting that those individuals who intend to do wrong are unlikely to be deterred by a code and that codes often express standards of behavior that should be inherent in a majority of the population. It was determined from the focus group responses that a clear understanding of dual use research is pivotal to assessing the value and impact of a code of conduct. In conclusion, many individuals agreed that a code would be an effective tool to raise awareness about dual use research in the life sciences.

Next steps for the working group will be to complete the draft code, taking into account the work products other NSABB working groups are developing and also to ensure broad public input on the process.

Discussion

Dr. Levy asked about the makeup and location of the focus groups. Mr. Nance said that the focus groups were formulated with the objective of obtaining the broadest and most accurate representation possible. Alan Shipp, Director of Outreach and Education for the Office of Biotechnology Activities (OBA), explained that because focus groups are inherently qualitative, the makeup of the groups was not a scientific sampling but rather a cross-section of the potential users of the product. Members included individual scientists, IBC members, and senior research administrators. Graduate students were not included, said Mr. Shipp, but would constitute an important community on which to test the code. Participants in the focus groups were drawn from various geographic regions of the country.

Dr. Keim advocated for the coordinated use of focus groups and workshops to obtain feedback on all of the NSABB work products. Mr. Nance agreed, saying that coordination of efforts

across all NSABB workgroups will be very important. Dr. Patterson underscored the preliminary nature of the workgroups' reports and the importance of broad input and careful consideration of these efforts by the public and the scientific community. To that end, she said, a strategic plan will be formulated for outreach that will address the education needs for codes of conduct and other NSABB activities in a coordinated fashion. Mr. Nance remarked that part of the charge to the Code of Conduct Working Group is to create a culture of responsibility which can only be accomplished through education.

Dr. Casadevall mentioned the likelihood that the code will need to be introduced at a relatively early age, possibly in high school, or whenever individuals are ready to conduct biological research. Mr. Nance confirmed that the working group has heard this sentiment from groups already in the process of developing training packages intended for both students and teachers at the high-school level. Dr. Rubin suggested that the book *Forbidden Knowledge*,[4] by Roger Shattuck, addresses many of these issues and might serve as a reference point. The book discusses the value of codes in medicine, such as the Hippocratic Oath. Other Board members agreed that codes can be a powerful mechanism to create cohesion and solidarity in a professional community.

An unidentified audience member asked how the NSABB is looking at the broader question of education in terms of disseminating knowledge about the subject area of Select Agents. Dr. Keim replied that education is an important priority for the Board. Dr. Patterson informed the audience that education and training are specific tasks in the NSABB charter. She invited creative ideas about education from the audience. She stated that there will be a later phase of broad education, outreach, and training when the workgroups' products on criteria and codes are developed and vetted through public comment. In addition, she said, the educational process is an important mechanism for the public and the research community to provide feedback on these draft products. Dr. Kasper observed that it might seem premature to form an Education Committee at this juncture, but broad consideration of the issues ahead reinforces the need to initiate education and outreach efforts sooner rather than later. Dr. Keim echoed this sentiment and also observed that obtaining buy-in from international groups for which the Board has no direct oversight or control can be made easier with a systematic educational mechanism.

WORKING GROUP ON SYNTHETIC GENOMICS: STATUS REPORT
David Relman, M.D.

Dr. Relman stated that the Working Group on Synthetic Genomics was primarily formed to examine the potential biosecurity concerns raised by the laboratory synthesis of Select Agents. The group has also been charged with the much broader task of examining the impact of synthetic biology on biosecurity and to make possible recommendations for strategies to address these concerns.

Dr. Relman began by explaining that conventionally, viruses can be rescued from recombinant or cloned DNA derived from the natural source of the agent itself. The emerging techniques of

[4] Shattuck R. Forbidden Knowledge: From Prometheus to Pornography. New York: St. Martin's Press, 1996. ISBN 0312146027.

reverse genetics have expanded the possibility for generation of viable viruses from their published sequences, bypassing the need for a natural source. Although the use, possession, and transfer of Select Agents are tightly controlled, the availability of DNA synthesis technology introduces new concerns with respect to the laboratory synthesis of these agents. Specifically, synthetic genomics allows the synthesis of these genomes de novo and thus potentially expands the number of people who might now have access to some Select Agents, as well as the means by which they may have received these agents.

In pursuing the issue, Dr. Relman reported, the working group received briefings on the existing legal framework for control of Select Agents, the current technological capabilities for synthesizing nucleic acids, and the state of the science for some key application areas that may be used to derive infectious agents from synthetic nucleic acids. He briefly summarized the group's findings in each of these areas.

Legal Framework

The Select Agent Rules implement the provisions of the USA PATRIOT Act of 2001, as well as the Public Health Security and Bioterrorism Preparedness and Response Act of 2002. These regulations set forth requirements for the possession, use, and transfer of Select Agents and toxins. Another particularly relevant law is 18 USC 175c, which makes it unlawful to knowingly produce, synthesize, or engineer variola virus, the causative agent of smallpox.

Of these laws and regulations, the Select Agent Rules is most relevant to the group's charge. These rules pertain to possession, use, transfer, and importation of agents in the United States. These rules do not explicitly address issues having to do with export from the United States. Dr. Relman said that the Export Administration Act has some applicability in this area.

Synthesis Technology

Reagents and equipment for synthesizing DNA are readily available around the world. Dr. Relman noted that synthesizing oligonucleotides of up to 120 nucleotides is routine and common, whereas synthesizing those of 180 or more is somewhat of an art. The technology to completely synthesize certain viral genomes is currently available. Not all DNA companies currently have this capability, but the ability is rapidly advancing. DNA synthesizers are available on eBay for a few thousand dollars. Thus, the technology is becoming increasingly available to individuals through increasingly compact, conveniently packaged, and automated technology and hardware. A recent article in *New Scientist*[5] reported the results of a survey of 12 biotechnology companies asked whether they screen orders for DNA sequences that might pose a bioterrorism threat. Five of the companies said that they screen every sequence received, four said that they screen some sequences, and three admitted not screening sequences at all.

[5] Aldhous P. The bioweapon is in the post. New Scientist, November 9, 2005, No. 2525, p. 8. Available at http://www.newscientist.com/channel/opinion/mg18825252.900.html. Retrieved May 15, 2006.

State of the Science

It is possible—and, in some laboratories, routine—to recover and/or reconstruct infectious virus sequences from DNA for certain Select Agents. Vaccine researchers have created infectious chimeric viruses using combinations of genomic material from various Select Agents. Scientists have expressed concern that attempts to regulate synthetic genomics may impede scientific progress in these critical areas.

Preliminary Conclusions

Dr. Relman reiterated that the Select Agent Rules constitute the legislation that is most relevant to the workgroup's charge. These rules regulate genetic material encoding for Select Agent toxins and also regulate genomic material that is inherently infectious and capable of producing a Select Agent virus. This applies regardless of whether the material is obtained via de novo synthesis or through traditional methods. In terms of biosecurity, the basic concern is that synthetic genomics may make it possible for an individual to acquire a Select Agent outside of these rules.

Dr. Relman explained that this concern arises from issues having to do with both scientific advances and industry practices. The concerns arising from scientific advances pertain to the rapidly expanding ability of an increased number of individuals to acquire and use readily available starting materials and procedures to synthesize infectious agents or toxins that may encompass certain Select Agents. In terms of industry practices, the lack of standard practices among vendors of synthetic nucleic acid is confounded by the lack of a widely accepted, optimized methodology for performing screening of orders that can be used by providers to ensure biosecurity.

Dr. Relman stated that the spirit of the Select Agent Rules is clearly intended to apply to individuals who synthesize DNA with the expectation that these persons know the identity of the material they are synthesizing. However, there are no explicit phrases or clauses within the rules that specifically require manufacturers of nucleic acids to know whether they have a Select Agent in hand. Dr. Relman observed that the rapid evolution of science and technology has given rise to a clear need to clarify the legal scope and interpretation of the Select Agent Rules as they pertain to synthetic genomics. There may also be a need to deliberate further on the adequacy of the current legal framework governing Select Agents and to explore a wide variety of strategies for addressing biosecurity concerns related to this form of science.

Next Steps

Dr. Relman reported that the workgroup will consider the need for criteria for the identification of Select Agents, as well as an outreach and education initiative for scientific and business communities to include guidance on their responsibilities under the Select Agent Rules. Other areas of consideration include the formulation of best practices for DNA synthesis providers and other measures to promote biosecurity in the field of synthetic genomes.

Action Items

The workgroup will collect additional information on the biosecurity concerns raised by the synthesis of Select Agents by engaging additional scientific experts, other groups working on related issues, and relevant international communities. The group will also refine their preliminary conclusions and develop recommendations for consideration by the Board as a whole. Dr. Relman invited the Board's feedback and suggestions on appropriate international parties with which the group might engage, how the findings of other groups relate to those of the Synthetic Genomics group, and any other issues that the Board would like to see the working group address.

Discussion

Dr. Casadevall pointed out that the working group will ultimately have to address the question of how a Select Agent is defined, and that this information is not currently available in the public domain. Dr. Dennis Dixon of NIAID reported that the Synthetic Genomics Working Group received a very helpful briefing from the Select Agent Program at CDC and that the CDC might be receptive to providing a similar overview for the entire Board. Dr. Kasper agreed that the Board should request a public briefing on the CDC's Select Agent decision-making process at the next NSABB meeting.

Dr. Franz asked whether the working group discussed the possibility that characteristics and classes of organisms should be used as the mechanism by which Select Agent lists are formulated, rather than genus and species names of specific agents, as was done in the 1980s and 1990s with the Department of Defense's Validated Threat Lists. Dr. Relman replied that the group discussed the possibility of incorporating functional features into some of the definitions, but it would be difficult to anticipate the functional characteristics of an agent that has been initially defined in terms of its primary sequence or other such attributes.

Other Board members concurred with the idea of departing from a list of specific agents and focusing more on the specific characteristics, uses, and outcomes of agents and organisms. Dr. Lemon pointed out that there are multiple lists used by the U.S. government (e.g., from the Public Health Service, the CDC, and the Department of Commerce), and that these lists are not identical. He noted that a single unified list would be a major advance.

DISCUSSION OF THE NRC REPORT "GLOBALIZATION, BIOSECURITY, AND THE FUTURE OF THE LIFE SCIENCES"

Stanley M. Lemon, M.D.
David A. Relman, M.D.

Drs. Lemon and Relman co-chaired the Institute of Medicine (IOM) Committee on Advances in Technology and the Prevention of Their Application to Next-Generation Biowarfare Threats, which recently released the report "Globalization, Biosecurity, and the Future of the Life Sciences." Dr. Relman began by reviewing the four charges to the committee (paraphrased here):

1. Examine current scientific trends and their likely trajectories on a variety of disciplines with respect to a number of possible consequences within 5 to 10 years; in particular, the impact of these trends and trajectories on applications that are relevant to the development of next-generation agents of biological origin, agents of bioterrorism or warfare.

2. Evaluate the potential for hostile use of these research advances, in particular, how these technologies might have a complementary or synergistic effect.

3. Identify current and potential future capabilities that might enable individuals, organizations, or others to acquire or master these technologies for both beneficial and hostile purposes.

4. Identify and recommend the knowledge and tools that would be needed by a variety of communities to anticipate, prevent, recognize, mitigate, or respond to the harmful potential of these technologies.

Dr. Relman began by outlining some differences between the IOM report and a previous report by the National Academy of Sciences' Fink Committee, which led to the establishment of the NSABB. He explained that the IOM committee was charged to look farther into the future and place greater emphasis on the global agenda. In addition, the IOM committee was asked to emphasize the impact of advancing technologies and to anticipate where current technologies are heading with an eye toward the types of technologies might emerge with some bearing on future threats.

The committee came to a number of conclusions through its discussions and explorations. These were that biotechnology is a powerful tool that is relatively inexpensive, and thereby carries the risk that it might be misused, either intentionally or unintentionally. It is based on publicly available materials and knowledge that are accessible and increasingly global in their distribution. In addition, recent advances in molecular biology and in understanding of gene control and how systems are regulated within the human body make it necessary to contemplate novel, manmade biological threats that may not have been immediately apparent after the events of September 11, 2001.

In many countries, particularly in developing nations, biotechnology has been heralded as a tool and a vehicle to promote economic and human development, which the committee thought to be appropriate. Most technologies are global in scope and are being adopted for economic use and basic investigation in many countries. Countries have widely varying goals with respect to their use of life sciences technologies and the specific path toward these goals differs greatly from one part of the world to another. For this reason, it s important not to assume that the trajectories of life sciences technologies can be interpreted globally through a limited assessment of a specific area of the world, such as the United States or Europe.

The committee was charged to examine many aspects of life sciences technologies and immediately concluded that it was impossible to be comprehensive. For this reason, the committee selected examples of technologies relevant to the charge in order to assess their

impact on future threats. To that end, the committee devised a classification scheme to better define the types of technologies under consideration. Dr. Relman invited Board members to provide input on the utility or effectiveness of this classification scheme. Dr. Lemon explained that in constructing the scheme, the committee intended to lay out a process by which one could continuously and iteratively examine the horizon for potential future threats without limiting the focus to a specific subset of threats or a specific list of agents. The committee also recognized that the threat spectrum will need to be reassessed frequently.

Dr. Lemon stated that, in agreement with discussions held during the Board's morning sessions, the committee felt that attention should not be constrained to a specific list of agents. In the future, there will be an ability to readily engineer non-pathogens into pathogens, so that the threat horizon is extremely broad and rapidly changing.

Drs. Lemon and Relman presented the five recommendations of the committee:

IOM Committee on Advances in Technology and the Prevention of Their Application to Next-Generation Biowarfare Threats: Recommendations

1. The Committee endorses and affirms policies and practices that, to the maximum extent possible, promote the free and open exchange of information in the life sciences.

2. The Committee recommends adopting a broader perspective on the "threat spectrum."

3. The Committee recommends strengthening and enhancing the scientific and technical expertise within and across the security communities.

4. The Committee recommends the adoption and promotion of a culture of awareness and a shared sense of responsibility within the global community of life scientists.

5. The Committee recommends strengthening the public health infrastructure and existing response and recovery capabilities.

Dr. Lemon reported that the committee discussed at length the importance of the open exchange of scientific information. He explained that embedded in the committee's first recommendation is the need to be sure that any rules and regulations that are established have a reasonable probability of contributing to a fix rather than to increasing the problem in some way. He stated that defining "dual use," in addition to the magnitude of the threat spectrum, should be an ongoing endeavor. In addition, he said, this is an international issue, and as such, the global scientific community must assume responsibility.

Discussion

Dr. Cohen asked Drs. Lemon and Relman how they saw the code of conduct being developed by the NSABB as being of particular utility toward meeting the IOM committee's recommendation number 4. He further inquired whether there might be some specific activity that might be undertaken jointly by the NSABB and the Biological Sciences Advisory Group. Dr. Lemon answered that the IOM committee's conversations about codes were parallel to the Board's morning discussion of the Code of Conduct Working Group's activities. The IOM committee

also considered how international, decentralized organizations might be constructed to promulgate the "culture of awareness" as well as serving as a reporting mechanism. He said that the IOM committee considered the possibility of formulating something akin to the Mayo Clinic's ProMed Web site, where the emergence of a new infection can be reported. The committee envisioned some type of Web-based system for making reports, comments, and criticisms that would be annotated and commented on by people in the scientific community. Dr. Franz brought up the idea of modifying some aspect of an existing system under the purview of an organization such as WHO. The Board members briefly discussed how such a parallel, ProMed-like system might function and how it might be evaluated.

Dr. Lemon stated that in all of the committee's discussions, there was a strong emphasis on the need to maintain foreign interactions and collaborations with foreign scientists. Restrictions placed on interactions with scientists abroad would negatively impact the U.S. scientific enterprise and also forfeit the opportunity to share the U.S. perspective and influence on a global scale.

COMMUNICATIONS WORKING GROUP: STATUS REPORT
Paul Keim, PhD

The Communications Working Group is charged with developing principles and tools that will lead to thoughtful, consistent practices regarding the responsible communication of information with dual use potential. Dr. Keim reported that the working group has had a series of conference calls as well as one face-to-face discussion and a panel discussion involving outside participants.

Dr. Keim noted the importance of consistency in the terminology used by all of the NSABB working groups, and that this requires interaction and coordination among the groups. He specifically cautioned against using the terms *biosecurity* and *dual use potential* interchangeably.

Dr. Keim noted that guidance and tools that facilitate consistent and well-considered approaches to evaluating communication are needed to publicly demonstrate that scientists recognize and are responsive to concerns about the security implications of their work. To that end, one of the Working Group's primary aims has been the development of a collection of overarching principles that can be used to guide the systematic and comprehensive evaluation of communications of research with dual use potential.

Overarching Principles

Dr. Keim summed up these principles as follows:

- Communication is vital for scientific progress.
- Research should be communicated to the fullest extent possible.
- A balance is needed between the benefits of research and its potentially negative aspects, between the risks and benefits of communicating information.
- A range of communication options should be considered; the decision to communicate information is not necessarily binary.

- Communication occurs throughout the research process and is a dynamic process.
- There is a need to consider what is communicated as well as the way in which it is communicated. The potential for public concern and misunderstanding should be minimized.

Assessment Framework

The working group has also developed a framework for identifying and assessing the risks and benefits of communicating dual use research information. The framework includes identification of the information to be communicated, identification and assessment of the risks and benefits of communicating that information, options for communication, and formulation of recommendations regarding communication. Dr. Keim noted that this framework could be used to review research proposals, manuscripts, presentations, and Internet postings and as an educational tool to raise awareness of issues surrounding dual use research within the scientific community and for ethics training. Anticipated users of the framework include scientists, students, institutional biosecurity review entities, reviewers of proposals and manuscripts, and government policy makers.

Dr. Keim provided an overview of the elements of the framework and then reviewed options that the working group formulated for communicating research identified as having dual use potential. These options pertain to the content, timing, and distribution of information, any of which can be modified in order to mitigate the potential for any adverse outcomes.

A communication plan is a critical part of the decision to communicate dual use research information. The working group has outlined a number of elements that are important to address when communicating information with dual use potential. These include the public health significance of the findings, the usefulness of the information to the scientific community, the biosafety measures that were in place as the research was conducted, the dual use aspects of the information, and assurance that biosecurity concerns were carefully considered in the decision to communicate. In this way, Dr. Keim noted, it may be possible to minimize the potential for sensationalism and overreaction.

Next Steps

The working group plans to seek broader input on the Overarching Principles and the Assessment Framework and revise them as necessary. Possible forums for public discussion include focus groups and workshops at professional meetings, the latter to be coordinated with other NSABB working groups. Dr. Keim stressed the importance of coordinating the efforts of all the NSABB working groups in this regard.

Dr. Keim noted a recurring finding from the Working Group's discussions with stakeholders, i.e. that many individuals in the life sciences community are not aware of the dual use issues and concerns. Dr. Enquist related an anecdote illustrating the general lack of awareness within the scientific community regarding the threats to biosecurity from dual use research and the ease with which individuals can be educated on this issue. Dr. Keim underscored the fact that a

significant portion of the scientific community has not bought into the importance of dual use research, reinforcing the need for education and outreach.

Discussion

Dr. Imperiale asked Dr. Keim to clarify the working group's thinking with respect to the risk/benefit assessment and the time frames referred to in the Assessment Framework ("immediate," "near term," and "long term"). He noted that it would be extremely difficult to assess the future risk or benefit of certain information. Dr. Keim responded that the group's intent was not to strictly categorize information, but to provide guidelines to encourage the reviewer to think about balance.

Dr. Lumpkin noted that use of the assessment tool relies on individual judgments and questioned whether this activity could be normalized to preclude subjective and value-laden evaluations of risk. Dr. Enquist replied that a similar but less formal type of risk/benefit assessment has been conducted since 2002 at the American Society for Microbiology (ASM). At present, he noted there is no way to assess the quality of an individual reviewer's judgment. Well-planned and -conducted outreach, however, can mitigate the extreme ends of the spectrum of opinion. Dr. Enquist related the process used at ASM to flag research with dual use potential and briefly described the Society's action plan for when such research is identified.

Dr. Osterholm expressed concern that research approved through extant oversight processes at the institutional level would be required to go through a second assessment process when a publication emanating from that research is submitted to a peer-reviewed scientific journal. Dr. Keim stated this would probably be the case and that the publishing journal would have the prerogative to reject a paper, even if the research passed institutional review for dual use potential. Dr. Osterholm noted that it would be beneficial to have a uniform, standardized review at both of these levels in order to preclude conflicting assessments.

Dr. Kasper expressed concerns for the prospect of instituting a review such as that outlined in the Assessment Framework at the institutional level. At a large university, for example, it would not be feasible to apply this assessment to every paper before it is submitted to a journal. Dr. Keim agreed and stated the most workable model would probably be self-identification and self-assessment at the level of the individual PI. He did not anticipate the framework as being a function of the IBC in any sort of formalized fashion.

Dr. Casadevall observed that the consequences could be disastrous if even one dual use paper compromised the nation's biosecurity. He said the primary goal of any such research review should be to prevent the release of any damaging information. Although a survey of papers submitted to ASM revealed that only three of more than 16,000 manuscripts required additional review for biosecurity reasons, Dr. Osterholm maintained that even this relatively small number is too high, since the goal should be zero. Dr. Lumpkin noted that the goal should be to identify biosecurity concerns throughout each step of the review process, so that the end result of the entire process is a product that has been fully considered and free of concerns. The redundancy and level of rigor exercised at each step should minimize any potential for error.

Dr. Erlick asked whether the working group has formulated a plan for placing potentially damaging information in perspective once it has been released. Dr. Keim said that the working group envisioned the communication plan as something to be implemented before, not after, publication, but that this was an excellent suggestion to bring back to the group for their deliberation.

Dr. Levy observed that when a paper is rejected on the grounds of a potential biosecurity or biosafety threat, the author could simply resubmit to another journal without revision. Dr. Nightingale noted a key to successful implementation of the plan would be targeting journal editors with a uniform instrument and a cohesive approach. He suggested that the assessment instrument could be improved if it were expanded to capture additional possible scenarios such as papers of such high risk that publication cannot be considered and discrete low-risk data available in the public domain that presents a significant risk when compiled. Dr. Lumpkin noted another element missing from the instrument is the way in which knowledge is created, i.e., through synthesis and creation rather than from original research.

Megan Davidson from the Southeast Regional Center of Excellence for Emerging Infections and Biodefense, reported that in May 2005 the Duke University IBC revised its protocol form to include the list of seven experiments of concern from the Fink Report. The form asks researchers whether there is a likelihood that their work would increase the pathogenicity of the organism on which they were working. To Ms. Davidson's knowledge, no researcher to date has answered in the affirmative. She cited this as an example of the limitations associated with allowing investigators to "self-police." As a result, her institution has implemented the model previously discussed, wherein RCEs have been designated to review research for dual use concerns.

Dr. Vidaver asked whether the working group considered entities other than academia that are conducting dual use research, such as non-government organizations and private industry. Dr. Keim replied that the peer review process is common across all types of organizations, so that the basic principles should translate across all sectors. Dr. Vidaver also asked whether the group had considered relying on publishers for reporting, rather than editors, whose positions at publications are transitory. Dr. Enquist stated that ASM has an editor-in-chief training program to maintain continuity between experienced and newly-appointed editors-in-chief and to provide updates on policies and procedures.

Dr. Osterholm asked whether the editor of a journal that has rejected a dual use paper has a duty to warn the institution from which the paper emanated of the potential danger associated with dissemination of the information. From a legal standpoint, Mr. Nance stated that if there is a foreseeable risk that can be reasonably prevented, the journal might have a duty to warn, but at present there is nothing in the criminal law specifically addressing that duty to warn specifically regarding dual use research.

WORKING GROUP SUMMATION
Working Group Chairs

Dr. Kasper asked the Chairs of the Working Groups on Dual Use Criteria, Communications, and Synthetic Genomics to give a brief summary of the future direction of their group based on the morning's discussions.

Dual Use Criteria Working Group
Dr. Kasper

- The wording of Question 2 in the Worksheet for Dual Use Potential will be reconsidered to determine whether it should be revised to set the bar higher for identifying dual use research of concern.

- The group will consider whether Question 3, concerning experiments in BSL-4 facilities, on the worksheet should be deleted.

- The group will attempt to more clearly define key terms, including *biosafety* and *biosecurity*.

- Outside input on the criteria will be sought from U.S.-based scientists and international scientists with NIH funding.

- The group will also discuss potential models that can be developed as systems for monitoring dual use research.

- The issues of weaponization and diagnostics are currently tabled; however, the group will reconsider these issues at some point in the future.

- The tasks of the working group will transition into the development of guidelines and oversight recommendations, using the risk assessment tool developed by the Communications Working Group as a framework upon which to base discussions of risk assessment in the guidelines.

Communications Working Group
Dr. Keim

- The group will complete its work on the Assessment Framework:
  - Feedback will be invited from the remaining NSABB members and outside individuals.
  - The assessment framework will be assessed for its applicability to other avenues of communication, such as web-based communications.
  - A cover sheet will be devised that provides some context for users. This will be submitted to the NSABB for feedback.

- The working group is identifying case studies that could be used as educational tools by the working group and in other applications.

- The group will assemble a panel of experts in the area of patents to present an informational session on the complexities of the patent process.

- The working group will also develop a concise, focused statement on the importance of communicating scientific findings in the life sciences.

- The group will discuss plans for a workshop as an opportunity to engage the potential users of the Assessment Framework.

- The working group will discuss how to engage in outreach and education for the scientific community as well as the public, the government, IBCs, and RCEs.

Synthetic Genomics Working Group
Dr. Relman

- The working group will focus on the question of whether existing regulations are adequate with regard to capabilities associated with synthetic genomics. Briefings with potential stakeholder communities, including scientists and others whose work may be affected by dual use research regulations, will be held in May 2006.

- The group will examine the impact of the field of synthetic biology on biosecurity issues.

- Input will be obtained from the authors of a Sloan Foundation study that involves groups from the Massachusetts Institute of Technology, the Center for Strategic and International Studies, and the Venter Institute to learn about the efforts of those institutions with regard to dual use issues. The group will develop recommendations based on the outcome of these discussions.

INTERNATIONAL PANEL: PERSPECTIVES ON DUAL USE LIFE SCIENCES RESEARCH

Introduction of Panel
David R. Franz, DVM, PhD

Dr. Franz stated that the NSABB was formed to provide advice to the U.S. government but that the potential for misuse of biological technology extends around the world. Although the Board can have little impact on the international community, it can help to foster international awareness and collaboration on the issue.

The International panel has begun several initiatives. It is currently seeking an opportunity to work with U.S. embassies in other nations to find points of contact, in both government and the international scientific community, with appropriate individuals who are willing to engage in a dialogue about dual use research. Dr. Levy, co-chair of the International Working Group, is president of the Alliance for the Prudent Use of Antibiotics and has offered to contact some of

his international colleagues to assess the current level of awareness about dual use issues in other countries.

Dr. Franz observed that biosecurity exists as a sort of spectrum encompassing biological warfare, biological terrorism, dual use, emerging disease, and chronic disease. Different nations may have different levels of awareness regarding the different points along this spectrum, and the issue may not be discussed frankly or openly in some circumstances. Dr. Franz emphasized the importance of sensitivity in regards to these issues during international dialogues.

Communication among the NSABB members and working groups, stated Dr. Franz, is equally as important as communication internationally. One of the goals of the NSABB is to develop recommendations to the U.S. government regarding how to foster international collaboration on effective oversight of dual use research. Dr. Franz pointed out that the process is as important as the product in this endeavor. Communication among scientists who are working together on very difficult problems builds understanding and trust, especially in terms of international efforts.

Life Sciences Research: Opportunities and Risks for Public Health
Ottorino Cosivi, DVM

Dr. Cosivi stated that the work of World Health Organization's (WHO) Department of Epidemic and Pandemic Alert and Response is to verify and respond to disease outbreaks. Most of the outbreaks to which the Department has responded in the past have been naturally occurring, such as tuberculosis and malaria. Others have been due to laboratory accidents, such as severe acute respiratory syndrome (SARS) in Singapore, Taiwan, and China in 2003–2004; ebola in Russia in 2004; and tularemia in the United States in 2004. In comparison, bio-risks from deliberate use or misuse are relatively rare and are thought of as low-probability, high-consequence incidents. The Department addresses all of these types of outbreaks in four phases: prevention, preparedness, response, and recovery.

The global coordination and leadership provided by WHO has contributed to control in the spread of diseases. The third edition of WHO's *Laboratory Biosafety Manual* was published in 2004 and addresses the general issue of dual use research. The Department is also formulating guidelines to assist countries in developing their own guidelines for this issue.

WHO's interest and involvement in issues of global biosecurity date back to 1967, when the World Health Assembly issued its resolution on the beneficial uses of human science. WHO's "Health Aspects of Chemical and Biological Weapons" was first circulated in 1970. The Report of the Advisory Committee on Health Research issued the report "Genomics and World Health" in 2002, which acknowledged the potential misuse of genomics for biowarfare and summoned the research community to take a proactive stance. Most recently, in 2002, WHO's resolution 55.16, "Global Public Health Response to Natural Occurrences, Accidental Release, and Deliberate Use of Biological, Chemical, and Radionuclear Material," stemmed from events surrounding September 11, 2001.

From a public health perspective, research and advancements in the life sciences provide both benefits and risks. Control mechanisms that are not well designed could hinder future

developments. It is important for the scientific and public health communities to maintain strong public confidence and to provide direction and sound scientific advice to policymakers.

Dr. Cosivi briefly reviewed his organization's perceived risks for the public health community if the issue of dual use research is not assessed in a thoughtful and comprehensive manner. These include the possibility that poorly designed control systems will interfere with the availability of new and beneficial knowledge; that over-regulation will stifle research and the opportunity to develop countermeasures; and that tightened controls might affect the conduct of life sciences research and distort the fundamental mechanisms for disseminating information. The questions and challenges currently under consideration include whether current measures are adequate to manage risks, whether regulations can be used to manage risks without hindering the benefits of life sciences research, and whether consistency can realistically be expected among the wide array of proposed control measures. WHO is pursuing the issue of laboratory biosecurity as a starting point to foster overall responsible conduct in biomedical research and development.

Dr. Cosivi reported that WHO has been exploring the global security implications of research and development efforts in the life sciences through a grant from the Sloan Foundation. The study will review certain types of life sciences research in terms of development, related techniques, and associated risks; opportunities and risks for public health; and the risks associated with misuse of these areas of life science research. Phase 1 of this study was completed in 2005.

In Phase 2, a study group comprising 14 to 16 international members will conduct regional seminars to test some general assumptions regarding global biosecurity. Dr. Cosivi acknowledged the broad background against which WHO posits these issues is beneficial and expressed hopes that the organization and others can serve as a platform for the Board's continuing discussions.

Discussion

Dr. Levy asked the extent to which most developing countries are seeking guidance from WHO on this issue. Dr. Cosivi replied that WHO is proactively engaging many countries of all stages of development.

Managing Risks of Research Misuse Associated with Grant Funding Activities
David Carr

Mr. Carr provided an overview of work in progress to help prevent risks associated with dual use research, sponsored by the Wellcome Trust and the United Kingdom's Biotechnology and Biological Sciences Research Council (BBSRC) and Medical Research Council (MRC). The BBSRC supports basic and strategic research in biotechnology. The MRC supports research across the medical sciences and in related areas. Both organizations provide funding through research grants to a number of institutes in universities throughout the United Kingdom. The Wellcome Trust supports research in all areas of the medical sciences.

In 2001 and 2002, growing concerns about dual use research caused the United Kingdom to introduce new antiterrorism legislation that gave the government increased power to restrict the use and transfer of potentially hazardous materials, including those of relevance to the life sciences. In addition, the U.K. government, through its Foreign and Commonwealth Office, chaired the 2005 discussions of the Biological Weapons Convention, focusing on the possible role of codes of conduct for scientists. Leaders of these efforts held a series of stakeholder discussions involving organizations with interests in this area in the United Kingdom, including the Wellcome Trust, the BBSRC, and the MRC. Mr. Carr pointed out that a number of U.K. organizations, including the Royal Society, the British Medical Association, and a number of other academic policy research groups, have longstanding interests in this area and might serve as future points of contact for the NSABB.

Mr. Carr stated that the U.K. government is highly conscious of the changes that have taken place in the United States in the wake of the 2001 terrorist attacks and has recognized that these changes have affected the funding and regulation of U.S. science. He noted that the Fink report played a major role in shaping the United Kingdom's thinking and policy on these issues. In light of these political developments, the Wellcome Trust, the SSBRC, and the MRC have each developed their own individual position statements on the misuse of biological research by terrorists. These three position statements are very similar, and are all based on a set of core principles:

- Appropriate systems must be in place to assess the risks of research misuse, but the risk must be considered in light of the benefits associated with allowing the research to proceed.

- The dissemination of research outcomes, particularly through scientific publication, is crucial to the scientific enterprise and should not be regulated by governments.

- International collaboration and training are important in the conduct of life sciences research.

- There is a critical need for the scientific community to actively develop systems of self-governance for the management of risks associated with research misuse and to support these efforts by actively seeking opportunities to raise awareness of these issues among its members.

- The Wellcome Trust, the SSBRC, and the MRC are committed to examining their grant funding procedures to address the risks of research misuse.

All three organizations have rigorous processes in place to ensure that research they support is of the highest scientific quality and conforms to high ethical standards. The core of the funding decision-making process for these organizations is peer review. Applications are sent out to a number of international reviewers who assess the applications' quality and consider ethical, social, and other issues pertinent to the request. As a condition of award, the institution that receives funding must take responsibility for ensuring all regulatory requirements relative to the research are met. The three organizations also have additional advisory mechanisms to address

issues not normally covered through standard ethical review procedures and offer guidelines on good research practice as well as policies to address alleged research misconduct.

Mr. Carr explained that the Wellcome Trust, the SSBRC, and the MRC are committed to work in partnership and examine how these already rigorous procedures can be strengthened, especially in light of concerns about research misuse. The ultimate goal of this partnership is to develop a consistent policy approach across the three organizations, representing the largest funders of life sciences research in the United Kingdom.

To that end, the three organizations conducted a joint consultation with members of their funding and advisory committees and developed a discussion paper setting out options for amendment of the organizations' grant funding procedures. The suggestions ranged from developing more explicit guidance to actual procedural changes. Feedback was received from 32 members across the three organizations, including life scientists in a wide variety of disciplines as well as members of expert committees and advisors on the ethical and social implications of research. In general, the responses indicated that there is universal recognition that the misuse of life sciences research is an important issue although additional layers of bureaucracy in the grantmaking process to address this issue are not undesirable. There is also strong support for developing explicit guidance on these issues with recommendations for small procedural changes for use by both applicants and reviewers.

In addition to the consultation exercise, a joint workshop was held with the Royal Society in October 2004. This event brought together U.K. life scientists and experts in the policy community to generate broader discussion of issues around research misuse. The outcome of all of these consultations was the development of a joint policy statement by the three organizations. Mr. Carr referred the audience to the copy of this statement included in their binders. The policy statement set forth four changes that will be introduced across the three organizations:

1. Guidance for applicants: Addition of a question on application forms asking whether the researcher has considered any risks of harmful misuse of the proposed research, what these risks are, and how the researcher intends to manage them

2. Guidance for reviewers: Explicit mention of research misuse as an issue to consider during review of the application

3. Guidance for funding committees: Clear guidance on the process for assessing cases in which concerns are raised

4. Good practice guidelines: Modification to include specific mention of the need for both individual researchers and their institutions to consider these issues on an ongoing basis

Through these changes, the three organizations hope to identify and assess potential risks at the application stage. Equally important is the hope that the changes will contribute to awareness-raising more broadly in most of the communities that receive funding from the three organizations. Ideally, both scientists and their institutions will continue to consider research misuse they go forward with their research efforts.

For the most part, the changes are still in the process of being implemented; however, the three funding agencies realize these changes alone are not sufficient to prevent research misuse and additional processes, such as good governance at the institutional level, will be critically important for successful oversight. The final change was instituted at the Wellcome Trust in late 2005 and it is still too early to determine its full impact, but initial reactions from the first round of applications suggest that applicants do not object to the additional request for information. The three organizations are committed to monitoring and reviewing these procedures and to participating in future policy discussions with groups such as the NSABB to share information and help guide the development of improved policies.

Dr. Carr closed by briefly mentioning the upcoming meeting of the U.K. Royal Society in September 2006, where international experts will convene to consider scientific developments of relevance to the Biological Weapons Convention.

Discussion

Dr. Kasper asked if the question about research misuse recently added to grant applications is part of an overall educational process for scientists. Mr. Carr explained this change to the application procedure is anticipated to contribute to wider discussions and awareness raising, which contributes to scientific education and understanding about the issues.

In response to a question from Dr. Franz, Dr. Carr stated that about 10% of funding from the Wellcome trust goes to institutions outside the United Kingdom.

Dr. Patterson referred to work being conducted by Malcolm Dando and colleagues on the development of a code of conduct that relates to dual use research concerns. She asked whether an education program has been launched in the United Kingdom and whether detailed guidances for investigators on how to answer questions concerning the potential for misuse are available. In addition, she inquired whether there have been cases identified as dual use research of concern and how they were handled. Last, she asked whether the three organizations' guidelines address the issue of communication. Mr. Carr replied that there is a critical need for education on the issue of research misuse in the United Kingdom, although the three organizations have not launched an educational program to date and he is not aware of a coordinated effort in that country. With regard to identified cases of dual use, he noted that there has been one such case at the Wellcome Trust that occurred before the changes were introduced. This application concerned research involving the manufacture of synthetic peptides that mimicked botulinum and tetanus toxins for the delivery of therapeutic molecules into nerve cells. The proposal came before the Trust's advisory group on ethics, where it was nearly unanimously decided that the benefits of the research outweighed potential risks. When the proposal was funded, there were no specific conditions placed on the research other than the usual grant conditions and best practice conditions. The Trust did, however, inform a government agency associated with the Chemical Weapons Convention that the proposal had been funded. With regard to Dr. Patterson's final question, Mr. Carr stated that there is nothing specific in the organizations' guidance regarding communication. The Trust's original position statements on terrorist misuse of research contain paragraphs emphasizing the importance of self-governance and the need to raise awareness

which broadly apply to communication. The Wellcome Trust intends to engage in additional policy discussions on this issue, but has not developed specific guidance on communication to date.

Report on "International Regulation of Biology"
Barry Kellman, JD

Mr. Kellman emphasized the following 10 points in his talk:

1. The term *international*, as it has been used throughout the day's discussion, extends beyond the concept of other nations. A distinction should be made between reaching out to other nations and to individuals who are not Americans, in terms of reaching the entire international community. The biotechnology and bioscience communities are proliferating widely in regions considered as our close allies and in parts of the developing world.

2. There are as yet no universal criteria for "dual use research of concern."

3. There is currently no process for an oversight mechanism, whether a criteria review, a methodology review, or an administrative procedure of review. Similarly, the rights and responsibilities of those being reviewed have not been established.

4. It has not been determined if a relevant reference group has implemented a code of conduct regarding dual use research that can be adopted throughout the research community. Communication and education are extremely important in efforts to adopt a code, since these activities help to reach individuals who might otherwise be overlooked.

5. Scientific issues evolve over time, whereas a code tends to be fixed. Codes that are very specific become outdated more quickly. A standing review mechanism for the evaluation of specific methodologies is important to retain the utility of a code.

6. Existing codes, guidelines, and ethical statements on dual research rarely consider the developing world. There is a general lack of recognition that biosciences extend beyond the United Kingdom, Europe, and China to include countries that are less technologically advanced.

7. In Mr. Kellman's experience, the developing world is concerned about issues of dual use research in the context of the development of bioscience research.

8. Existing codes and guidelines do not allow the identification of individuals who intend to use life sciences research for nefarious purposes. Such individuals are not likely to abide by any code of conduct and are not likely to be identified through existing codes and guidelines.

9. The international community lacks a comprehensive requirement for nations to enact laws that require a license for the use of Select Agents and there is no global regulatory

body to supervise the conduct of bioscience. Unless that gap is filled, efforts will continue to be directed at only those individuals who can be trusted and ignore those who cannot.

10. Communication between the scientific community and international law enforcement agencies, specifically Interpol, would be a major advancement in establishing a mechanism for the prevention of bioterrorism. Mr. Kellman offered to convey the Board's interest in collaborating with Interpol should the Board like to pursue such a partnership.

Discussion

Dr. Kasper asked Mr. Kellman to clarify the nature and role of Interpol. Mr. Kellman replied that Interpol is a freestanding international organization of national police forces representing nearly 200 countries. It was set up to act as a coordinating body and serves as a mechanism for nations to cooperate in terms of law enforcement. Interpol recently established a program on the prevention of bioterrorism, funded by the Sloan Foundation. A large international conference was held in 2005 in Lyon, France, where Interpol is based, and was attended by 600 people from more than 160 countries. Since then, the organization has held two regional workshops, one in Cape Town, South Africa, and one in Singapore. A third workshop will be held in July 2006 in Chile. There are plans to hold a fourth workshop by the end of 2006 for Russia and the states of the former Soviet Union.

Dr. Kellman further recommended the establishment of a reporting mechanism that would offer a way to obtain current information on bioscience research. Such a mechanism would complement the promulgation of codes of conduct and guidelines intended for dual use research that are distributed to the research community, by providing an opportunity for the community to respond back to the authorities. Currently the bioscience and biotechnology sectors are growing faster than the laws intended to oversee these activities without the benefit of any feedback mechanism.

Dr. Rubin observed that the "Achilles heel" underlying the theory of engaging the international community is the junction between biodevelopment and biosecurity. The developing world does not view the issue of biosecurity as consistent with their need and desire to engage in development processes. Dr. Kellman disagreed with this last point, saying that the developing world instead views an insistence on biosecurity as consistent with an interest in global development. As a result, this is where bioscientists can take a leadership role in promoting efforts that foster the development of bioscience in developing countries while emphasizing the importance of biosecurity.

Dr. Levy observed that the role of NSABB is not directly related to law enforcement, but instead focused on raising awareness of dual use issues in the scientific community, particularly among young scientists. Dr. Kellman agreed that the Board's role is not to identify criminals and detect criminal activity; however, there are many other options available for the interchange, communication, and collaboration of the scientific community and the international law enforcement authorities.

Dr. Lemon speculated whether there might be an opportunity for a program in the life sciences, such as President Eisenhower's Atoms for Peace initiative. Dr. Kellman replied that he believed similar opportunities are available to advance some type of global covenant for biosecurity. He offered that the goals of the Millennium Development are an excellent framework for these types of issues.

Enhancing Biological Security with International Cooperation
Terence Taylor

Mr. Taylor began by expressing his belief that scientists should be engaged transnationally to raise awareness of risks that might arise from rapid advances in the life sciences as well as from the natural environment. Through a "bottom-up" process, researchers in the life sciences can help to promote best practices, norms, and guidelines that ultimately find their way into legislation, rules, and regulations.

Extraordinary advances in the life sciences and biotechnology bring enormous benefits to medicine, public health, and agriculture. At the same time, the risk to public safety and security from the misuse of science and technology must be minimized by the active involvement of the life sciences community.

The spectrum of biological risks ranges from those that occur naturally to accidents and misadventure and even deliberate misuse. The hazard lies not in the use of weapons and dangerous pathogens, but also in the lack of a shared global language, methodologies to assess risk, and universal standards in biosafety and biosecurity. In addition, these present similar challenges to traditional multilateral institutions, individual scientific organizations, and national governments.

The International Council for the Life Sciences (ICLS), which Mr. Taylor directs, was created in December 2005 to help enhance biosafety and biosecurity through the promulgation of international standards and the sharing of best practices. The organization is the product of more than 3 years of intensive work around the world in which private, academic, and public sectors were equally engaged. The Council's mission is to "help ensure global health, safety, and security by safeguarding the opportunities offered by advances in the life sciences and their application through the promotion of best practices, standards, and codes of conduct."

Language choice is extremely important in talking about dual use and misuse. Part of the ICLS mission is to increase global awareness through a global network. In his experience and that of his colleagues, there is a readiness to demonstrate responsible behavior with regard to life sciences research by the international community. In particular, countries that are relatively new in the biotechnology arena aspire to measure up to global standards. ICLS is initiating a training system to better refine these standards. As yet, there is no internationally recognized system that can be referenced and ICLS hopes to fill that gap.

In certain countries and governments, a bridge between the government and the private sector maintains international contacts. This illustrates the direction taken by some nations, which

recognize the transnational nature of bioresearch and the need for academic, private, and commercial players to interact with all associated governments. For example, Mr. Taylor noted examples of how biosafety and biosecurity issues are approached in some countries:

United Kingdom: The United Kingdom represents one end of the spectrum. The Health Protection Agency spans across various government departments rather than acting as a single department. It serves health protection from the standpoint of safety and security in the areas of biological, chemical, and radiological research.

European Union: The European Microbiology Organization and its sister laboratory may serve as a key point of entry for international dialogue, since they place a high priority on the issues of biosafety and biosecurity. This agency has previously interacted with ICLS and may provide a possible avenue for partnership.

Singapore: In 2005, Singapore introduced a national network and is developing a commercial center with government support. The deputy prime minister is the focal point for national security coordination and is also the chairman of the Ministerial Council on the Life Sciences. Singapore serves as an example of how biosecurity and commercial interests have interfaced with academic activities, resulting in a unified national center for life sciences research and advancement.

India: The Confederation of Indian Industry has a Biotechnology Committee in its pharmaceutical section that would serve as an appropriate point of contact to obtain insight into their philosophy toward biosecurity. India is highly motivated to comply with current global standards in training, safety, and security as a way to achieve international recognition and approval in their biotechnology pursuits for reasons previously discussed.

Russia: ICLS, together with the Moscow Medical Academy, will host a seminar on enhancing biosecurity and biosafety. The G-8 presidency is currently in Russia and served as the primary incentive to host this seminar. It is critical to engage new and younger scientists and students in Russia into the biosecurity process.

Saudi Arabia: At a recent research conference, Mr. Taylor met a representative of the Saudi Arabian food and drug authority. This individual noted that although Saudi Arabia currently has no regulations for biosafety and biosecurity, there is a keen interest in cooperating with ICLS. This example illustrates the other end of the spectrum, where little or no regulation exists.

Examples of global approaches used to raise awareness and promote biosecurity issues were cited. These include the Biological and Toxin Weapons Convention, WHO, G-8 and global partnerships, the Inter-Academy Panel, and global networks of life scientists such as the World Federation for Culture Collections. All these entities represent valuable points of entry for engaging in an international dialogue.

The role of the ICLS is to help develop the necessary partnerships with policymakers, the public, academia, and industry in order to provide a forum and a focal point for the sustained

engagement of the life sciences community, as indicated by the ICLS charter provided to members.

Discussion

Dr. Keim noted that NIH and other agencies of the U.S. government have a history of imposing guidelines and regulations on foreign laboratories where they provide funding for research. For example, the CDC funds certain research at the Institut Pasteur and inspected this site for compliance with its standards. Mr. Taylor was asked to speculate how such regulatory requirements would be received in developing countries, which are dependent on external funding for research activities related to specific diseases significant to their populations. He suggested that such requirements could be implemented through an agency experienced in international collaborations, such as ICLS, and noted that the specific language used and the manner in which regulations are imposed will ultimately affect the success of such endeavors, although most developing countries have an earnest intent to meet international standards.

Dr. Relman asked about potential points of leverage within private industry that are based in the life sciences and whether these might present opportunities for engagement of partners in the developing world. Mr. Taylor noted one obvious route would be through trade associations, such as the Biotechnology Industry Organization (BIO). For example, India and Australia have demonstrated that cooperation between their respective trade associations have fostered international recognition of their efforts. It is important that the appropriate agency initiate such discussions and ICLS hopes to facilitate the creation of a global network with private industry, government representation, and academia.

Dr. Lemon noted that certain Select Agents of great concern to biosecurity in the United States may be endemic and very common in some developing countries. He asked whether these countries hold the same biosecurity concerns. Mr. Taylor replied that biosafety and biosecurity should be discussed together and there should be a common language and common methods for risk assessment. He noted that the National Academies would benefit from a multidisciplinary group working on this issue. Dr. Keim noted that this is a significant limitation in the use of agent lists, since such lists are extremely country specific.

PANEL DISCUSSION
All session speakers

Dr. Keim began the question-and-answer session by asking panel members to discuss the importance of resources in developing countries as a factor in engaging their interests in dual use issues. Dr. Cosivi noted that the perception of risk and the level of importance placed on dual use research are very different in developing countries compared to the United States. A different approach must be used to attain the same goals.

Dr. Nightingale asked Dr. Cosivi to speculate if he envisioned opportunities to engage developing countries during the implementation phase and building capacity of the International Health Regulations. Dr. Cosivi explained that the original International Health Regulations were

issued in 1969 and covered essentially three agents: plague, yellow fever, and cholera. In 2005, these were revised and approved by the World Health Assembly to become effective in July 2007. The new regulations have two primary changes. First, they require member states to cooperate with WHO in responding to threats that represent a public health risk of international importance. This stipulation is not limited to specific diseases, but instead is broad in scope. Second, countries must meet minimal standards with regard to biosafety and biosecurity. This second requirement serves as a strong point of leverage and could be used to engage those countries.

An unidentified audience member inquired about the relationship between NSABB and the law enforcement community, specifically the Federal Bureau of Investigation (FBI) and the Department of Justice (DOJ). It was noted that the law enforcement community has a strong interest in NSABB's deliberations. The FBI and DOJ will serve as partners to convey NSABB's recommendations about biosecurity throughout the law enforcement community, both domestically and internationally through partnerships with Interpol and others, including the more than 50 international attaché field offices.

Another unidentified audience member asked Mr. Kellman about his efforts, working through the United Nations (UN) to develop an international instrument that would criminalize possession of certain biological agents. Mr. Kellman cited UN Security Council Resolution 1540, prohibiting the development or use of weapons of mass destruction and calling upon nations to adopt effective measures to control materials and other items that might be used for the development of such weapons. He noted that most countries are moving toward criminalization of their use, but that some countries enacting laws in response to UN Resolution 1540 fail to understand there may be some instances of possession which are legitimate. In these cases, the legislative response exceeds the basic requirements needed for protection.

Dr. Franz asked the panelists for suggestions on how the Board might gather a broad data set related to dual use research that reflects international concerns. Mr. Taylor said that a global networking system would be crucial to this effort and that opportunities must be available for people to interact in order for an international culture of responsibility to be developed. These types of efforts require planning and coordination, so interpersonal contact is critical.

Future Plans

Dr. Levy said that the panel discussion was enlightening for the Board and that it was particularly instructive to hear about the activities in progress in other areas. NSABB's goal, in terms of international outreach, is to identify appropriate individuals and groups to serve as points of contact for NSABB workproducts in other areas of the world, especially developing countries. He stressed the importance of the international effort and potential partnerships with some of the groups that participated in the afternoon session.

Dr. Franz said that the panel discussion helped the Board to frame the problems and issues they face. Furthermore, it will be extremely important for the International Working Group to maintain close contact with the new Education and Outreach Working Group that is being

established for NSABB. Moving forward, the Board can continue to define its mission within the context of building collaborative relationships internationally in this manner.

PUBLIC COMMENT SESSION

Gerald Epstein
Center for Strategic and International Studies

Mr. Epstein referred to an earlier discussion of whether the wording in the threshold criteria formulated by the Dual Use Criteria Working Group should be changed from "…could be…misapplied" to "…would be…misapplied." He advocated to keep the word *could* since he felt this language would send a more direct message that the Board's intent is to minimize any likelihood that dangerous information will be made available to the wrong individual(s) and would help to minimize potential problems with public perception of biosecurity. He also noted the need to be proactive when the public perceives a problem with certain types of research. Finally, referring to the earlier discussion of whether criteria ought to address system issues, he referenced the NSABB charter which states that the Board's function is "to provide advice, guidance, and leadership regarding oversight of dual use research, defined as biological research." Given this objective, systems research falls outside the purview of the NSABB.

David Silverman
Director, Health and Safety Program, Stanford University School of Medicine

Mr. Silverman applauded the Board's efforts, particularly in regard to education, communication, and outreach. He asked the Board to also consider the need to maintain other programs in the NIH Office of Biotechnology Activities (OBA), such as guidance and oversight for the more than 600 IBCs across the country. As a community member of the IBC at the University of California, San Francisco, Mr. Silverman said that IBCs rely on OBA for advice and guidance. Mr. Silverman also noted that law enforcement agencies can sometimes overreact in situations with only the perception of wrongdoing and that more hand-holding and less wrist-slapping would be more appropriate in these situations.

ADJOURNMENT

Dr. Kasper thanked all those present for their participation and adjourned the meeting at 6:00 p.m.