# National Science Advisory Board for Biosecurity (NSABB)
# Meeting Minutes
# November 21, 2005
# Bethesda, Maryland

## Committee Members

Dennis L. Kasper, M.D., NSABB Chair
Murray L. Cohen, Ph.D., M.P.H., C.I.H.
Honorable Susan Ehrlich
Barry J. Erlick, Ph.D.
David R. Franz, D.V.M., Ph.D.
Claire M. Fraser, Ph.D.
General John A. Gordon (Ret.)
Michael J. Imperiale, Ph.D.
Paul S. Keim, Ph.D.
Stuart B. Levy, M.D.
John R. Lumpkin, M.D., M.P.H.
Adel A.F. Mahmoud, M.D., Ph.D.
Mark W. Nance, J.D.
David A. Relman, M.D.
James A. Roth, D.V.M., Ph.D
Harvey Rubin, M.D., Ph.D.
Thomas E. Shenk, Ph.D.
Andrew A. Sorensen, Ph.D.
Admiral William O. Studeman (Ret.)
Anne Vidaver, Ph.D.

## Ex Officio Agency Representatives

Louisa Chapman, Ph.D., White House Office of Science and Technology Policy
Brenda A. Cuccherini, Ph.D., M.P.H., Department of Veterans Affairs
Dennis Dixon, Ph.D., NIH/National Institute of Allergy and Infectious Diseases
Anthony S. Fauci, M.D., NIH/National Institute of Allergy and Infectious Diseases
Maryanna Henkhart, Ph.D., National Science Foundation
Peter R. Jutro, Ph.D., Environmental Protection Agency
Sue Haseltine, Ph.D., Department of the Interior
Dale E. Klein, Ph.D., P.E., Department of Defense
Terry L. Lomax, Ph.D., National Aeronautics and Space Administration
Boris D. Lushniak, M.D., M.P.H., DHHS/Food and Drug Administration

Janet K.A. Nicholson, Ph.D., DHHS/Centers for Disease Control and Prevention
Stuart L. Nightingale, M.D., Department of Health and Human Services
Elizabeth George, Ph.D., Department of Homeland Security
Caird E. Rexroad, Jr., Ph.D., U.S. Department of Agriculture
Anthony F. Rock, Department of State
Scott Steele, Ph.D., Department of Justice
David G. Thomassen, Ph.D., Department of Energy
Vincent L. Vilker, Ph.D., Department of Commerce
Ronald A. Walters, Ph.D., Intelligence Community

National Institutes of Health Representatives

Elias Zerhouni, M.D., Director, NIH
Amy Patterson, M.D., Director, NIH Office of Biotechnology Activities

Guest Speaker

Mike Leavitt, Secretary, U.S. Department of Health and Human Services

NIH Staff Members in Attendance

Allison Chamberlain, OBA, OD
Kelly Fennington, OBA, OD
Mary Groesch, OBA, OD
Susan Harper, OBA, OD
Kathryn Harris, OBA, OD
Brendan Keegan, OBA, OD
Minerva Rojo, OBA, OD
Michelle Saylor, OBA, OD
Allan Shipp, OBA, OD
Ansalan Stewart, OBA, OD

Call to Order

Dennis L. Kasper, M.D.
NSABB Chair
Harvard Medical School

Dr. Dennis Kasper, Chair of the National Science Advisory Board for Biosecurity (NSABB) welcomed members, the public, and individuals watching via webcast to NSABB's third meeting. He introduced new member Judge Susan Ehrlich of the Arizona Court of Appeals. Judge Ehrlich previously served as an Institutional Biosafety Committee (IBC) representative at the University of Arizona and is a candidate for a Master's of Law in Biotechnology and Genomics at Arizona State University. Dr. Kasper also introduced and welcomed two new ex officio members. Mr. Anthony Rock represented the Department of State. He is the Acting Assistant Secretary of the Bureau of Oceans and International Environment and Scientific Affairs. Dr. Louisa Chapman is the new Assistant Director for Life Sciences in the White House Office of Science and Technology Policy.

Dr. Kasper led a roundtable of introductions by all members and ex officios. He noted that Board members Arturo Casadevall, Stanley Lemon, Michael Osterholm, and Diane Wara could not be present and introduced the day's first speaker, Dr. Elias Zerhouni, Director of the National Institutes of Health (NIH).

Opening Remarks

Elias Zerhouni, M.D.
Director, National Institutes of Health

Dr. Zerhouni stated that NSABB was formed to advise on core issues in dual use research, i.e., life sciences research undertaken for legitimate scientific and public health reasons that has the potential to be misused to threaten public health and other aspects of national security. He noted that the Board faces the challenge of balancing the protection of the public with the advancement of science and said the key organizing principle is the need for a greater culture of responsibility among scientists.

A fundamental policy challenge described by Dr. Zerhouni relates to decisions on diffusion of knowledge. The complexity of this issue was evidenced not long before, when the sequence of the 1918 influenza virus was published. Dr. Zerhouni said the benefits of making the sequence available to hundreds of laboratories committed to the good use of life sciences research outweighed the risks. He said that researchers, research administrators, policymakers, and scientific publishers must regularly take a fresh look at research findings and technologies and ask these fundamental questions: What is the risk-benefit threshold? If there is a potential for misuse, what measures can be taken to safeguard against harm?

Dr. Zerhouni said the Board is asking the life sciences field to help by providing practical

guidance and tools that can help identify research that has dual use potential. He emphasized the importance of developing criteria to clearly define dual use research. Until these criteria are in hand, there is some risk that a critical subset of life sciences research could become stigmatized. Dr. Zerhouni acknowledged that scientists direct their work where opportunities lie, and in many cases will not allow themselves to be subjected to undue restrictive burdens. Yet he stated that many researchers he had spoken with feel a heightened sense of responsibility to contribute in these new areas of science. He asked the Board to consider the creation of positive incentives to prevent stigmatization.

Dr. Zerhouni said the code of conduct that will emerge from the Board's work will probably be the first line of defense and the best means of fostering a culture of responsibility within the life sciences. The Secretary of HHS, NIH administration, and numerous others will look to the Board for guidance on the sharing of scientific results and technologies. He said that NSABB must manage a system of research that is complex, and in many ways, unpredictable in its essence. He noted a key lesson that emerged from the work of the Recombinant DNA Advisory Committee (RAC), which was to include the scientific community in their proceedings. Dr. Zerhouni stated that the Board's recommendations should arise from a process of inclusion and participation, so that ultimately there is not only a new culture, but buy-in for the new culture. Stakeholders in the life sciences community must be consulted early and often to ensure that policies and practices are appropriate to the task, feasible, practical, and effective. In addition, public consultation should be a recurring theme as recommendations for the Secretary on dual use research are developed. The RAC was characterized by a widespread use of public consultation, which created momentum and support for a fledgling field of research that was considered high-risk in the minds of many.

Dr. Zerhouni summarized by emphasizing the following points: 1) There is no absolute threshold at which one can determine an appropriate risk-benefit ratio; 2) A culture of responsibility is the main goal and should be widely disseminated at the level of local research; 3) Inclusion and participation are key to ensuring that these new cultural norms are implemented; and 4) The Board's advice will be sought in specific areas because some aspects of dual use research will have to be carefully restricted.

Dr. Zerhouni introduced the Secretary of the Department of Health and Human Services, Mr. Mike Leavitt.

## Opening Remarks

Mike Leavitt
Secretary, U.S. Department of Health and Human Services

Mr. Leavitt stated that the U.S. is considered a leader in medical and scientific research. Private industry and U.S. taxpayers, through institutions such as NIH, spend billions of dollars on research every year. He related an experience at a recent ministerial meeting with 48 other countries. The room became quiet when Mr. Leavitt began to speak because everyone turned

their attention to hear what the United States had to say.

Mr. Leavitt said that those who sent anthrax to the Brentwood Post Office probably did not receive training in the context of terrorism. He said they were undoubtedly trained in the context of science or medicine, which illustrates why the topic of dual use research is critical. Scientists are in a precarious position, because lives depend on the breakthroughs they make. Yet every experiment and scholarly article must be looked at through the "eyes of a bad man." Although the country is committed to the open sharing of scientific information, materials, and technologies, the U.S. is also committed to preventing potentially dangerous dual use research from reaching those with the intent to cause harm. Mr. Leavitt said the Government can't and shouldn't police every experiment or review every article. Rather, an ethic must be developed in the life sciences that balances the interests of national security against the compelling need for scientific advances. NSABB was formed to help achieve this balance by advising the Government and recommending strategies for efficient and effective oversight of federally conducted or supported biologic research. He said the Board brings together a wide variety of expertise in national security, biodefense, law, ethics, food, the pharmaceutical industry, academia, and the publishing industry. Mr. Leavitt thanked the Board for their rapid response in reviewing the manuscripts on the reconstruction of the 1918 influenza virus. He said their advice was extremely helpful in guiding the actions taken and that the Board will be called upon again in similar situations.

Mr. Leavitt stated that international collaboration will be necessary to ensure the successful oversight of dual use research. He asked the Board to develop strategies for fostering international collaboration in an increasingly networked world and said actions taken by the United States alone will not be sufficient. Mr. Leavitt closed by stating that he looks forward to receiving recommendations from NSABB and that he highly values the Board as a resource.

Chair's Remarks and Agenda Overview

Dennis L. Kasper, M.D.

Dr. Kasper reviewed the activities planned for the day. Dr. Amy Patterson would provide an overview of NSABB activities, followed by a report from each of the NSABB working groups concerning their deliberations up to that time. He urged all members to participate in the discussions that would follow. Dr. Kasper added that in conjunction with the report of the Working Group on Communication of Dual Use Research, he would provide a brief summary of the closed NSABB meeting that took place in September of 2005.

Overview of NSABB Activities: Current and Future

Amy P. Patterson, M.D.
Director, Office of Biotechnology Activities, NIH

Dr. Patterson said the products developed by the NSABB working groups would be first steps

toward development of a comprehensive framework for the oversight of dual use research. She reviewed the NSABB charge, stating that the Board was asked to develop criteria for identifying dual use research, a code of conduct for researchers, policies for the responsible communication of dual use research, guidelines for both local and Federal review and oversight, training and education programs, and strategies for international coordination and collaboration. At the inaugural meeting in June of 2005, the Board formed four working groups to address criteria development, a code of conduct, communication, and international collaboration. The Board was also asked to identify and assess biosecurity concerns raised by the rapidly evolving field of synthetic genomics. Dr. Patterson stated that this working group was being launched and would report at the next NSABB meeting.

Dr. Patterson said that the individual working groups are aware that their tasks and work products are relevant to those of other working groups. Ultimately, all the work must come together in a cohesive, flexible framework for the oversight of dual use research.

The first working group was scheduled to report on dual use criteria. Dr. Patterson said their task was to deliberate on questions such as: "What is dual-use research? How will we know it when we see it?" She said that life sciences research that doesn't meet the criteria developed will not be subject to further dual use review, while projects identified as having dual use properties will be examined carefully. A given dual use project may fall anywhere along the spectrum from low- to high-risk, and it is anticipated that many projects will be deemed fairly low-risk and exempted from further review. Dr. Patterson said the tasks of risk management and risk assessment are integral parts of the review process and that the Board would be turning its attention to these areas in the coming year.

Dr. Patterson stated that that the research process is not a simple, discrete activity with a predictable linear progression to a certain outcome, but rather, a complex array of activities. The process is iterative and is carried out by people from many disciplines, often distributed around the globe. She said these properties of the research process have important implications for the working groups' products.

The codes working group is examining the responsible conduct of dual use research. Dr. Patterson stated that the adoption and implementation of an effective code of conduct will require buy-in from those engaged in all areas of the research process, ranging from the investigator to scientific administrators at the local, Federal, and international levels. She said the communications working group noted that communication occurs at multiple points in the research process. The publication of a manuscript is preceded by many opportunities for poster presentations, seminars, and other works in progress. Therefore, principles for responsible communication must be embedded in the code of conduct and apply throughout the research process. Dr. Patterson stated that because science has become an increasingly global endeavor, the international group is tasked with developing strategies for early and frequent engagement with other countries for the cooperative oversight of dual use research. Once draft criteria, a code of conduct, principles for responsible communication, and strategies for international collaboration are in place, the Board will then focus on review processes, principles for risk

assessment and management, training and education, local and Federal oversight, and ultimately, the development of guidelines.

In closing, Dr. Patterson underscored that the Board is facing considerable challenges with very high stakes. They are trying to minimize biosecurity risks while also minimizing unnecessary burdens to the research enterprise. She stated that scientists did not previously need to be concerned about the potential malevolent misuse of their findings and now it is an extremely important concern.

Dr. Patterson stated that the working groups took a measured approach to their respective tasks, staying mindful of potential unintended consequences. She said that broad consultation and a thorough vetting of each proposed element of the oversight framework will be necessary to help ensure that the results are sound and effective.

Dr. Patterson then described the conflict of interest requirements that apply to all special government employees (SGEs), including the Board members. The rules and regulations are explained in the report titled, Standards of Ethical Conduct for Employees of the Executive Branch, which was received by Board members upon appointment to the Committee. Dr. Patterson stated that Board members must be attentive during meetings to issues that could arise that affect or appear to affect their interests in a specific way. In such cases, Board members are asked to recuse themselves from the discussion and to physically leave the room. Dr. Patterson said that questions about the rules of conduct or conflict of interest should be referred to Ms. Kimberly Caravello.

Dr. Kasper introduced the working groups' progress reports.

Working Group Progress Report: Criteria for Identifying Dual use Research and Results

Dennis L. Kasper, MD, Chair

Dr. Kasper chaired the working group established at NSABB's inaugural meeting with developing a set of draft criteria for the full Board's consideration. Dr. Kasper shared the group's thinking to date and asked for feedback from NSABB members.

As a starting point for deliberation, the working group looked at existing definitions of dual use research, such as the basic definition in the NSABB charter, i.e., "dual use research is biologic research with a legitimate scientific purpose that may be misused to pose a biologic threat to public health and/or national security." Dr. Kasper noted that much more detail and precision is necessary to allow for consistent determination of dual use research, which is critical for instituting uniform and systematic oversight programs.

The working group's approach was to explore the full range of possible criteria that might be used to delineate dual use research, keeping in mind several key considerations. One deals with the fact that life sciences research is a dynamic field that encompasses many diverse disciplines.

Ideally, the criteria will be relevant to each new scientific capability and technology that arises as life sciences progresses. Dr. Kasper noted that there is a simultaneous and compelling need for the criteria to be sufficiently specific to ensure that they capture only that research that is dual use and requires specific oversight. As it's unlikely that any criteria could accomplish all of these goals perfectly, it will be important to periodically review the criteria and modify them to ensure their relevance as technology advances. It may be appropriate to exempt certain dual use research from further review, but there must be criteria or parameters for delineating that subset of research. Dr. Kasper said this task might fall outside the scope of the working group's activities and may be addressed in the future by those developing draft oversight mechanisms.

Some research and information that might be considered dual use is already subject to specific regulations and oversight. This includes Select Agents, recombinant DNA, and certain exports. These areas should be considered during the development of oversight mechanisms to avoid duplication or contradiction.

Dr. Kasper stated that a designation of research as dual use simply means that it may warrant special consideration regarding conduct, oversight, and communication. It does not mean, a priori, that this research should not be conducted or that the findings should not be communicated. The working group had also discussed the premise that although biomedical research brings many benefits, the possibility of associated biosecurity risk must be considered when developing criteria. The comparison of level of risk versus degree of benefit is important for determining whether future oversight is warranted.

The working group concurred with Dr. Zerhouni's point that that broad public input is essential to the development of useful, comprehensive criteria at the initial development stage, as well as during future reassessments.

The working group considered two components of research that may serve as a starting point for further criteria development: 1) The intrinsic properties of an agent used in the research; and 2) The experimental procedures and manipulations that take place. The working group focused on four broad categories of research that capture the range of areas in which dual use potential may exist.

The first category is research with specific agents with high potential for posing a biologic threat to humans, animals, or plants, such as Select Agents. However, the term "agent" must be further defined, and could include microbes, biologic agents, infectious agents, microorganisms, toxins, and other compounds of biologic origin. The parameters of dual use research should not be limited to research involving Select Agents, but should include other potentially harmful agents. Toward this end, the working group considered some of the properties used in making decisions about which organisms and toxins should be designated as Select Agents, including the degree of pathogenicity, environmental stability, communicability, ability to genetically manipulate the organism, available treatment, and ease of dissemination.

The second and third categories of dual use potential could increase an agent's potential for harm

and could enhance the susceptibility of the host to harm. For both of these categories, the working group looked to the seven "experiments of concern" outlined in the National Research Council (NRC) report, *Biotechnology Research in an Age of Terrorism*. Dr. Kasper listed the seven experiments of concern, which may:

- Demonstrate how to render a vaccine ineffective;
- Confer resistance to therapeutically useful antibiotics or antiviral agents;
- Enhance the virulence of a pathogen or render a non-pathogen virulent;
- Increase transmissibility of a pathogen;
- Alter the host range of a pathogen;
- Enable the evasion of diagnostic or detection modalities; or
- Enable the weaponization of a biologic agent or toxin.

Dr. Kasper noted that these types of experiments represent a starting point, but will likely be modified over time.

The fourth category in which dual use potential may exist would encompass other research findings or technologies that could be misused to pose a biologic threat to humans, animals, and plants (a "catch-all" category). The working group used the phrase "enabling technologies" to describe research that could, for example, be used in the weaponization of biologic agents. Additionally, "facilitating information" was described as that which identifies vulnerabilities in public health and safety, such as mathematical models of threat scenarios. Information that could enable the synthesis of a dangerous pathogen would also fall into this category. The working group considered whether laboratory equipment should be considered a component of dual use research, but did not propose this as a parameter. Generally, laboratory materials are widely available and highly specialized equipment is not always needed to perform basic techniques. In addition, the export of certain laboratory equipment is already regulated by the Department of Commerce.

Dr. Kasper said that criteria could be developed from the general categories he described. He emphasized that not all research that falls into these categories would automatically be dual use, but dual use research would likely come from these categories.

Dr. Kasper moved on to the topic of whether risk assessment techniques could help identify dual use research. Since risk assessment has been applied in developing the Select Agents list, it might be a useful tool. However, further evaluation is needed to determine its applicability.

For next steps, the working group proposed that they evaluate the applicability of the criteria used in identifying Select Agents. They will also further assess the NRC list of experiments of concern and modify it as necessary. They plan to further define the "enabling technologies" and "facilitating information" categories and their applicability to dual use research. The working group plans to consider additional modifications based on factors such as the economic and public health impact of possible misuse of the research and the relevance of research activities outside of the life sciences. They will further examine the utility of the application of risk

assessment and the most appropriate stage of research evaluation for its use. Finally, the working group will consider the development of parameters for dual use research that do not warrant further review or can be exempt from additional review.

Dr. Kasper asked the Board for comments on the proposed categories of research developed by the working group

Discussion

Dr. Paul Keim said the Select Agent list is an obvious place to start, but cautioned the working group to keep in mind that it has a political history that reflects the practicality of implementing severe regulatory oversights. He recommended not being restricted to that list, but rather, looking at guiding principles that will help to determine whether an agent falls into the category of dual use. He stated that the list could be a "quagmire" that could trap the Board, rather than effectively guiding the process. Dr. David Relman agreed. Dr. Keim clarified that he was not suggesting that the working group revise the Select Agent list, but he said the threat for dual use is broader than the list, and therefore the Board should propose broader guidelines. He said, as an example, that the Select Agent list is severely limited in the agricultural area.

Dr. David Franz noted that the first and the fourth categories are lists, which will be easier to implement. The other categories are principles, and therefore harder to implement. He said they are related in many ways to intent. He agreed with Dr. Keim that the Board shouldn't fall into a trap of doing what is easy. Development of principles will be the most effective way to deal with the problem, but also very difficult.

Dr. Keim asked if the working group had discussed who will decide where the principles apply and by what means. Dr. Kasper said that is an active area of discussion. The initial feeling was that they be applied using some form of simple checklist to be completed by the individual investigator. Research that raises concerns about possible dual use would be sent to the local IBCs for consideration and a more significant risk assessment.

Dr. Claire Fraser noted the need for assessment along the entire spectrum of research, from concept through to publication. She asked how the responsibility for risk assessment would shift as research moves through the process. Dr. Kasper replied that input is needed from multiple working groups so that this area can be clearly defined.

Dr. Relman said there could be value in considering research that seeks to exploit or reveal critical vulnerabilities. He also suggested considering what would fall within the exempt category at an early point in the working group's deliberations.

Dr. Barry Erlick stated that there must be a very close association between the dual use research working group and the communications working group because it's not possible to know what agent may pose a risk in the future. The risk may not become clear until it's time to publish.

Dr. Stuart Levy recommended that the working group use examples in their guidelines to help investigators understand dual use research in a concrete way.

Dr. Harvey Rubin asked how tightly basic research can be tied to the end technology. He said it is critical to define emerging technologies as the firewall between basic science and dual use. He asked where this technology barrier should be placed. Dr. Kasper agreed that there are clearly some technologies that have the potential for harm, although not invented for nefarious purposes. He acknowledged the difficulties in this area. He gave the example of the emerging technology of synthetic genomes, which will have dual use research implications. Dr. Kasper said a subcommittee would probably be formed to deal with those recommendations.

Dr. Tom Shenk raised the issue of sign-on at an international level. He asked when the appropriate time would be to solicit input on dual use research from outside the U.S. Dr. Kasper stated that there is tremendous interest in the Board's work at the international level and that Dr. Franz was scheduled to speak specifically about international issues later in the day.

Working Group Progress Report: Codes of Conduct for the Life Sciences

Mark Nance, J.D., Chair

Mr. Nance stated that formation of the Codes of Conduct Working Group responded to the NSABB charge to provide recommendations on the development of a code of conduct for scientists and laboratory workers that can be adopted by professional organizations and institutions engaged in the performance of life sciences research. At the inaugural meeting of the Board, the charge was expanded to include the development of standards and principles that can be included in a formal educational and training program to promote appreciation for codes of conduct in the life sciences. Mr. Nance said the working group may be asked to advise the Federal Government, through the Board, on issues related to the conduct of research that may have dual use characteristics.

Significant accomplishments for the group included the development of a work plan and background reference materials for the full Board, several organizing and planning meetings conducted via conference call, and a full-day meeting on October 20, 2005 that included presentations from invited speakers who are considered luminaries in the field of ethics and the responsible conduct of research. These speakers provided information on the demonstrated value of codes in the scientific and professional fields, ways to enhance receptivity for a code of conduct within the life sciences community, and underlying principles to use when drafting a code. One of these principles underscores the importance of including the target audience as participants at the outset of the development process. The experts also addressed the effective introduction of codes into existing core areas of instruction and methods to assess the impact of codes, similar to those used to evaluate the success of Responsible Conduct in Research (RCR) training programs. Lastly, they presented on the need to consider the international aspects of a code during its development.

The working group's research activities included reviews of applicable literature, reviews of codes from other organizations and disciplines, and reviews of proceedings from international efforts. The group then identified basic premises that served as a starting point in considering the application of codes in a dual use context. They also developed some preliminary objectives, identified a target audience, and initiated a strategy for developing a code.

One key finding was that a code of conduct is an effective tool that can raise awareness about issues related to professionalism and sound practice within a given field. In the context of NSABB's activities, a code can be used to articulate primary issues of concern for the life sciences community and to communicate the responsibilities associated with dual use research. However, despite these positive outcomes, a code will not prevent intentional acts of bioterrorism and can't be expected to have a significant impact on individuals who are intent on violating social or professional norms or the law.

The life sciences community is already familiar with the use of codes in general because many scientific organizations and professional societies have adopted codes for their membership. Most codes are voluntary, but they promote a culture of responsibility by defining professional standards and expectations for their adherents. Once established, the responsibilities and duties outlined in a code become integrated into the culture to help maintain a level of self-regulation. For this to occur successfully, reinforcing activities, such as routine educational programs, are required. Mr. Nance noted that a universally accepted code has the ability to cross borders and influence international audiences.

Another important determination by the working group was that the success or failure of a code can be influenced by the appreciation of the code by its adherents. If the constituency develops a sense of ownership through direct involvement in code development, the process of introducing and indoctrinating the code is significantly facilitated. For this reason, the working group concluded that it would be ill advised to draft a code without soliciting input from the individuals and groups who would be expected to adopt it. Mr. Nance said the working group's initial efforts in 2006 will be focused on gathering feedback from recognized leaders in the life sciences to help guide their efforts.

Because the concept of dual use research as it relates to the life sciences is relatively recent, very few codes have elements that address dual use or the topic of biosecurity. However, the literature review indicated that several disciplines address security concerns. Mr. Nance stated that NSABB is not the only group considering a code of conduct to address biosecurity and dual use research in the life sciences. Efforts are underway by the Biological Weapons Convention (BWC), the International Council for Science (ICSU), the National Academies of Science (NAS), and others. Although their work is of interest to the working group, it would be premature to include them in NSABB's mission. Mr. Nance said that Dr. Murray Cohen would serve as a liaison with the international working group to track international activities of interest. He said the criteria under development will also ultimately impact recommendations for a code.

The working group developed a preliminary list of specific objectives for the code. It should

serve as a tool to increase awareness and understanding of the dual use potential of various research activities in the life sciences. The code should help promote a common language that standardizes concepts and vocabulary and establishes clear values and standards pertaining to biosecurity in the life sciences. The code should cross disciplines and reinforce the idea that the responsibility for biosecurity is shared by all those engaged in life sciences research. The target audience envisioned for the code includes a broad cross-section of individuals and groups participating in life sciences and biosecurity activities. These activities will not be limited to bench research, but will include such areas as communication, clinical research, and other efforts integral to the life sciences research process.

Since buy-in by the adherents is critical to success, Mr. Nance reported that the working group hopes to solicit stakeholder input to define relevant standards and values for a biosecurity code. They plan to accomplish this goal using three approaches. Initially, they will sponsor a meeting of invited thought leaders and luminaries in the life sciences to discuss the code. Next, they plan to participate in professional and scientific meetings as speakers and in workshops to exchange ideas and help garner support for the code among its constituents. Lastly, they will sponsor town hall meetings to encourage an open exchange of information with stakeholders.

Mr. Nance said that the next steps for the working group are to: 1) Develop an educational and outreach program with stakeholders to solicit input early in the process and educate constituents after the code has been introduced; 2) Identify standards and values applicable to a code for dual use research; 3) Develop a draft code for consideration by the Board; and 4) Consider procedures and methods to evaluate the code's impact on behaviors relevant to dual use research.

In his conclusion, Mr. Nance asked the Board to consider the following questions: Which stakeholder groups should be consulted on the development of a code for dual use research? Which professional societies and scientific organizations could offer the most useful opinions? Which professional societies and scientific associations should be targeted for subsequent outreach activities? What type of forum would facilitate the most effective exchange of information at professional meetings? Are there any other tasks or objectives the working group should consider?

Discussion

Dr. Andrew Sorensen asked if the working group had examined the idea of stipulating that adoption of the code is necessary to receive NIH, NSF, DoD, or other Federal funding. Mr. Nance replied that they had not yet addressed the issue.

Dr. Michael Imperiale asked whether the group had discussed the timing for individuals to be exposed to the code, e.g., students entering graduate school or medical school. Mr. Nance said they looked at the educational efforts already underway by other organizations, and based on their analysis, the working group advocates for exposure at a very early stage for those entering a life sciences field. Dr. Sorensen agreed that undergraduate students should be targeted. Dr. Kasper commented that the start of post-doctoral fellowships is a critical point in time. Dr. Levy

stated that in the medical profession, doctors are required to repeat courses and said that education is an iterative and ongoing process. He emphasized that it's very important to develop an educational process that will be positive and serve as a deterrent for those who might want to do harm. Dr. Rubin suggested that the working group also consider public relations with the general press to define the meaning of the code and clarify that it's voluntary.

Admiral William Studeman suggested developing a "straw man" code prior to collaboration efforts to sharpen the debate and outreach process.

Dr. Anne Vidaver asked if there should be discussion of the consequences of violating the code. Mr. Nance said that the working group plans to learn more about this issue from the scientific community. He noted, however, that the more severe and punitive the code is, the more difficult it might be to obtain buy-in from a community. He agreed, though, that without "teeth," the code would be ineffectual. He said the question to ask is, what form should those consequences take: persuasive, normative, or punitive? The review of the literature indicated that a threat of severe penalties is not necessary to modify behavior when dealing with highly educated people who are for the most part, sincerely interested in doing good. Most people engaged in this kind of research would view professional disapproval as a strong reprimand. Mr. Nance said the working group hadn't reached the point where they think punitive stricture is required.

General Gordon asked for more information about the other organizations that are developing biosecurity codes, particularly NAS, and asked how duplication of effort or competing codes could be avoided. Mr. Nance said that these organizations are in different stages of code development. As NSABB has a legislative requirement to develop a code, the working group must proceed within a specific time frame. However, they will be looking at the work of the other groups so that NSABB's efforts will be informed by them.

Dr. Franz commented on the approach of developing only one code and asked, from an international perspective, about the idea of developing a "code kit" that contains basic principles. Mr. Nance said the working group had looked at code kits promulgated by other organizations. They describe the most effective and essential components of a code of conduct, although not in the life sciences. This information had informed the working group's analysis.

Admiral Studeman said there are linkages in codes of conduct to legal and regulatory frameworks. He suggested a matrix showing how the code is linked to these frameworks, which might address the question of whether, under certain circumstances, there should be penalties or consequences as a result of codes violations. Mr. Nance said the working groups' research revealed that codes tend to exceed legal or regulatory limits. The law could therefore be considered the lowest common denominator.

Dr. Keim said he preferred to focus on a culture of ethics for the code, rather than on punitive measures. However, he pointed out that there is an enforcement capability at the publication stage. If journal editors and reviewers are in agreement with the code, they can enforce it then.

So that the Board could make recommendations on stakeholder groups to consult, Dr. Rubin asked what kind of data is needed from other organizations by the codes working group. Mr. Nance said that was part of what was being asked of the Board, i.e., "What questions do we need to ask?"

Admiral Studeman asked when the guidelines for local and Federal review and oversight and training and education should start. Dr. Patterson stated that these tasks overlap and blend into one another. She said that many of the questions being raised in the meeting must be answered before the content of the training and education programs and the guidelines are developed. She added that the Board's recommendations on guidelines and codes of conduct will be taken into consideration by the Federal agencies represented by the *ex officios*. For some of these agencies, the guidelines will become a term or condition of grant award. Adherence to a code of conduct or elements of that code may also become a term or condition of grant award.

Dr. Sorensen made a suggestion concerning the professional societies and scientific associations that should be targeted for subsequent outreach activities. He recommended contacting presidents and vice presidents for health affairs and vice presidents for research at universities. He said he could provide a list of associations of university presidents, university vice presidents for health affairs, and university vice presidents for research.

Summary of Second NSABB Meeting

Dennis L. Kasper, M.D.

Part of NSABB's charge is to advise on national policies governing publication, public communication, and dissemination of dual use research methodologies and research results. Dr. Kasper summarized the outcomes of the second meeting of NSABB, which took place in September of 2005 in a closed session to consider the publication of manuscripts about the reconstructed 1918 influenza virus. Because the manuscripts were unpublished at the time and were considered confidential, the Board's deliberations were closed to the public.

The Board was asked to advise on two papers in the process of being published, one in *Science* by Tumpey, et al., titled *Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus* and one in *Nature* by Taubenberger, titled *Characterization of the 1918 Influenza Virus Polymerase Genes*. The Communications Working Group met first, followed by the full Board. The key points of discussion were the significance of the information to the scientific community and public health, the risk of the information being misused, the benefits of communicating the information, and the consequences of restricting the information so that the public would not have access to it. The Board unanimously concluded that the public health benefits of these two publications far outweighed the risks or potential risks of misuse by persons with malevolent intent. The Board recommended that the papers be published.

As part of this process, the Board transmitted several recommendations to Secretary Leavitt.

One was that the manuscripts needed modifications to explain the health benefits of the research to the public. Another was the need to amplify the discussion of the measures taken to protect researchers and the public from accidental exposure or inappropriate access to the virus. The Board also recommended the development of additional Federal biosafety guidelines and a Federal regulatory framework for controlling access to the 1918 virus. Subsequent to these discussions, the virus was added to the Select Agent list. Lastly, the Board recommended development of a comprehensive communication plan for public dissemination of this type of information.

Discussion

Dr. Murray Cohen asked about the response to these recommendations within HHS and by the journals. Dr. Patterson said all the recommendations were adopted by HHS. The editorial boards appreciated the input, although they considered the timing of the request for the Board's review inconvenient. She said the experience underscored the importance of deciding where in the research continuum the communication plan should be considered and that it will need to take place much earlier. Dr. Patterson said there was a spectrum of responses from the general public. Some thought this was an example of responsible science and that dissemination was vitally important to national and international public health measures. At the other end of the spectrum, some felt the information should have been restricted.

Dr. Sorensen asked how Dr. Philip Sharp's editorial, written to accompany the *Science* article, was received in the scientific community. Dr. Patterson said that, based on the feedback she heard, it was well received. The issue raised awareness throughout the scientific community.

Working Group Progress Report: Communication of Dual Use Research Results, Methods, and Technologies

Paul Keim, Ph.D., Chair

Dr. Keim stated that the obvious place in which communication of dual use research comes to the forefront is in journal articles, which involves authors, editors, and reviewers. The working group emphasized, however, that there are many other points at which dual use scientific endeavors could be communicated and that it is important to consider them all.

Dr. Keim said that their charge was to examine the options and strategies for addressing issues related to the communication of dual use research information and to develop draft recommendations for NSABB. The working group examined the potential audiences for these strategies. They recognized that the audience is broad-based and includes students, researchers, laboratory directors, institutional review bodies, research administrators, and research sponsors, in addition to journal authors and editors.

Several deliverables were in progress by the working group, including overarching principles for responsible communication, a framework for assessing the risks and benefits of communicating

dual use research, principles and options addressing how and when to communicate information, and options for local review of products containing information with national security implications. A workshop on the communication of dual use research was being planned to bring together individuals such as journal editors, researchers, and representatives from funding agencies to obtain feedback on working group activities. To prepare for this workshop, the working group had been examining the existing systems and proposed models for the review and communication of work products that might have national security implications. These included Federal policies and relevant regulations, the policies of professional societies and scientific journals, and the practices of other disciplines that deal with the control of sensitive information.

The working group was in the process of developing case studies that would highlight the issues and could serve as test cases for their proposed approaches. The intent was to identify scientific communications that have dual use potential and develop written documents to illustrate how the principles, frameworks, and risk benefit tools would be applied. They had identified a series of scientific journal publications, websites, patents, and other communication mechanisms to use as test cases. They were also identifying outreach needs to support the development of NSABB recommendations and the dissemination and implementation of new policies pertaining to communication of dual use research.

Dr. Keim stated the working group was developing several overarching principles. The first principle was to communicate research to the fullest extent possible. This would permit the advancement of life sciences to benefit public health and the environment. They felt the restriction of scientific communication should be the rare exception rather than the rule. Dr. Keim stated that a working group survey of the American Society for Microbiology (ASM) indicated that only a very small number of submitted articles raise security concerns.

Another overarching principle described was the need for balance. The sharing of information and technologies that underpin scientific progress must be balanced with the need to mitigate the potential for deliberate misuse of information. Dr. Keim said that a small amount of misuse could be very damaging and could outweigh the benefits of information that is safely disseminated. However, there is in fact only a very small potential for misuse, while there is a tremendous potential for beneficial use.

Another overriding principle was that the decision to communicate a particular piece of information doesn't have to be a "yes" or "no" proposition. It might be possible to reach a compromise in the way the information is communicated, either in content or in tone. Therefore, it will be important to consider each communication in a way that will maximize the good and minimize the potential for misuse.

A point that came up continually in the working group's discussions was that communication doesn't occur at one point in time, but at multiple points throughout the research process. Dr. Keim said it is important to apply principles and practices of responsible communication throughout the research endeavor, well upstream of the publication stage. He displayed an

example of a timeline for scientific research that showed early project concept and design, application and award of funding, institutional approval, generation of data, and development of a manuscript or product. Ultimately, the manuscript or research product is released, but communication takes place throughout this entire process. Many of the activities along the spectrum, such as reviewing grants, giving presentations at national conferences, posting information on the Web, exhibiting student posters, and interacting with visiting scientists, are examples of points at which dual use research can be communicated. There is not one single portal for information.

Dr. Keim stated that it's important to consider not only what is communicated, but also the way in which information is communicated. Dual use information may raise biosecurity concerns in the general public and there is great potential for misunderstandings and sensationalism. Contextual or explanatory information can minimize misinformation and manuscripts can be modified to include more language describing public health benefits.

The working group had discussed the fact that life sciences research is dynamic. Misuse of a scientific paper or a scientific result is very unpredictable and there is a significant gray area. In addition, the scientific enterprise is global in nature and most publication takes place on the international level. Therefore, any rules governing dual use research in the United States must be accepted by the international community or they will not be effective. Dr. Keim said that for these reasons, the responsible communication of dual use research is an important value to incorporate into the code of conduct and in ethics training.

In addition to the principles outlined, the working group felt it was important to develop tools. One of the proposed tools would be a framework for assessing the risks and benefits of communicating dual use research products. Dr. Keim said that it would first be necessary to make an initial determination whether there is a risk to public health or national security. This could be a yes/no decision and if there is no potential for misuse, the product would be taken out of consideration. If there is a potential for misuse, it would be weighed against the potential for benefit. Factors that should be weighed include the introduction of novel scientific information or technologies, great potential benefit to public health or national security, and the time frame during which misuse is likely. For example, if, in the very near future, the product could be misused, that would weigh on one side of the equation. On the other hand, if the benefit from this information would be immediate and important, such as a vaccine to prevent a flu pandemic, the long-term potential for misuse would be outweighed.

Dr. Keim said the working group was developing spectrums of options for communicating dual use. He said it's important not to send the message that if research has dual use potential, it can't be published. Some research will have a potential for dual use and yet should be published. The working group recommended that communication plans be developed for research with dual use potential. It will be necessary to understand the possible consequences of a given paper and plan ahead to mitigate misunderstandings or sensationalism. The working group felt that public understanding and trust will be critical.

For next steps, the working group planned to continue working on principles for responsible communication. They were developing an algorithm for risk-benefit analysis, a set of communication options, and a document or tool that would help others develop communication plans. They were also preparing for the workshop scheduled for late winter.

Discussion

Dr. Sorensen noted that the communication of scientific findings in the scientific community will require a radical transformation of the culture because scientists are "semi-autonomous agents." He said they divest themselves of the responsibility for communication once their manuscripts are accepted for publication. He also asked how regulation of online journals would take place. Scientists may develop blog sites and blog on each other's work. He found the working group's goals commendable and noble, but struggled with understanding how they could be implemented. Dr. Keim agreed that the group is undertaking a very large task. He said great hope lies in the development of a culture of responsibility. He also expressed fears that draconian regulations might be deemed necessary unless changes are effected within the scientific community.

Dr. Claire Fraser said the Board has a limited ability to instill a culture of responsibility within the scientific community. She said the topics of most concern are often the ones that are of interest to the general media. She said that, in large part, it is up to the media to act responsibly and not sensationalize some of these issues. Dr. Keim acknowledged her point, but said they would do what they could to make sure the media is given factual information.

Dr. Imperiale asked whether there should be engagement of the public to determine their concerns and then develop communication methods to allay those concerns. Dr. Keim agreed and said they would include the public on the list of target audiences. General Gordon suggested adding policymakers and legislators. Dr. Keim agreed and said that was the thinking behind the term "research administrators." Dr. Vidaver suggested adding students of journalism and science writers to the list of target audiences.

Working Group Progress Report: International Collaboration

David R. Franz, Ph.D., D.V.M., Chair

Dr. Franz stated that the NAS report, *Biotechnology Research in an Age of Terrorism*, recommended harmonized international oversight. He read from the report, which stated that, "Any serious attempt to reduce the risks associated with biotechnology must ultimately be international in scope because the technologies that could be misused are available and being developed throughout the globe." Dr. Franz explained that the International Working Group was charged with recommending strategies to foster international collaboration on the oversight of dual use research in the life sciences. He said there is currently a lack of international consensus on the level of risk posed by the dual use life sciences, on the definitions and terminology relating to the oversight of biosecurity concerns, and on the legislative and regulatory frameworks needed for

controlling dangerous pathogens and toxins.

The working group's first meeting resulted in work plan objectives, draft operating principles, a preliminary inventory of global life sciences research expertise and capacity, a list of draft deliverables, and a list of liaisons who can keep the working group apprised of the needs of the other working groups and help with communication on an international level.

Dr. Franz described three work plan objectives: 1) To determine the current level of global expertise and capacity to conduct potential dual use life sciences research; 2) To develop a joint strategy with the other NSABB working groups to support their goals internationally; and 3) To raise international awareness and seek input from the international community. He said they would listen closely to international colleagues. The working group is in the process of identifying the stakeholders in international scientific societies, non-governmental organizations, and other entities. These efforts will help clarify how other countries perceive the threat of biosecurity. Dr. Franz said there are significant differences on this issue in various parts of the world. When more information is obtained, the working group will look at mechanisms to engage the scientific community in cooperative efforts.

Dr. Franz stated that the working group will be guided by the following operating principles: 1) The scientific enterprise is global in nature; 2) Scientific expertise is not uniformly distributed worldwide; 3) Effective oversight of potential dual use life sciences research requires international coordination; 4) Early and ongoing input and perspectives of other countries are key to success; 5) Balance must be maintained between protecting against the misuse of dual use technologies, while not limiting the good that can come from them; and 6) The process used to solicit cooperation from the international community may be as important as the product. Dr. Franz said that working together well, even if the resulting product is not perfect, may be a better outcome and afford more protection than a perfect product.

The deliverables proposed by the working group include an inventory of stakeholders, an inventory of countries conducting dual use research, workshops and conferences to solicit stakeholder input, a strategy for supporting the international dimension of the NSABB working groups, and recommendations to the Board for fostering international collaboration. Dr. Franz said they might develop a toolkit of information and concepts that could be shared with, but not forced on international colleagues. He emphasized that there must be true collaboration, not a "Made in the U.S.A." effort.

Dr. Franz noted that liaisons are designated for each of the other NSABB working groups. They will communicate the progress made in the other groups and report on the work of the international group. In closing, Dr. Franz asked the Board to consider whether there were other objectives and stakeholders that the working group should consider.

Discussion

Dr. Levy, as co-chair of the working group, reported that they had compiled a lengthy list of

countries that were interested in collaborating with NSABB. He said one of the challenges was to identify the "champion" in those countries, such as a professional society or individuals with influence. He said that reaching all the stakeholders that could have an impact is the foundation for success.

Dr. Relman wondered to what degree the working group considered sub-national, non-state parties, such as local organizations and international groups that don't necessarily respect national boundaries. Dr. Franz replied that most of their work centered around non-country stakeholders, in addition to international organizations such as WHO, scientific organizations, and national and international academies.

Dr. Keim agreed with the point that the process is more important than the product, and he suggested that all the working groups include an international representative in their workshops.

Dr. Erlick asked how much of the Board's work would be shared internationally on an ongoing basis. Dr. Franz said there was no specific plan, but that those issues were under consideration. Dr. Levy added that the workgroup wanted to avoid the impression that NSABB is trying to work in secret. They are being open and letting it be known that international scientific groups are part of the process. Dr. Erlick expressed concern that some groups might inadvertently be excluded and regard these efforts suspiciously, perhaps seeing NSABB as an attempt by the U.S. to control their research.

Dr. Kasper asked what overseas colleagues were expecting from NSABB and what they might be worried about. Dr. Franz said he had been hearing positive reactions, such as some input received from WHO. He stated, however, that the reactions probably vary. While some nations don't have any concerns, others might worry that the U.S. will try to impose restrictions on other countries' scientific communities. For example, they may worry that NSABB's work will affect international funding from NIH. He said the risks and benefits are different for different countries, especially concerning developing countries versus developed countries.

Dr. John Lumpkin suggested coordinating the working groups, so that more than one workgroup could ask questions of the same people. Dr. Kasper agreed with this idea.

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Dr. Levy noted that other international groups are developing codes of ethics and asked about the status of efforts to partner with them. Mr. Nance said there is a great deal of good work already underway and the Codes of Conduct Working Group planned to draw upon the best ideas of other international groups and incorporate them. They had been in direct and indirect contact with some of these groups, as had some of the *ex officios*. Dr. Levy emphasized the need for this effort to be seen as involving countries other than the U.S.

<u>Public Comments</u>

Unidentified Commenter
CSE

The first commenter said there are many common issues and challenges that link the four distinct working groups. He felt it was important to identify those common themes to avoid duplication of effort. He suggested a matrix to compare and link many of the issues as overlapping challenges. Ultimately, there could be common deliverables or initiatives at the national or international levels. He asked how a common platform could be achieved among the various countries with different perceptions of biosecurity issues. He stated that if the effort is viewed simply as a threat perception issue, it will not be unifying. He suggested framing the issue as a set of challenges that science and research and development efforts are facing as a whole.

Elisa Harris
Center for International Security Studies, University of Maryland

Ms. Harris acknowledged the four broad categories of research described by the criteria working group to help guide researchers in determining whether their work is dual use. She agreed with Dr. Levy that it's important to move from those broad general categories that could encompass almost all life sciences research into specific guidance for researchers and review committees.

Ms. Harris described her work at the University of Maryland on managing the risks of dual use research. It has involved scientists, lawyers, ethicists, and security experts. They tried to break consequential research into three broad categories of highest risk, moderate risk, and lowest risk. Within each of those categories, they identified specific types of experiments that they believe ought to be subject to oversight, either locally, for the work that poses the lowest risk, or internationally, for the work that poses the highest risk. In the middle range, there is a national oversight and review requirement.

She stated that at the highest level of oversight, they include de novo synthesis of an eradicated agent, such as the 1918 influenza virus. At the moderate level, they have a list of eight different types of experiments, including work with a newly discovered agent and increasing the virulence of a listed agent. They draw on the Select Agent requirements, but recognize that if there were to be an internationally harmonized system, international agreement on the list would be necessary. At the lowest level, they include increasing the virulence of a non-listed agent.

Ms. Harris' team has developed ideas that are very specific concerning the type of work that should be subject to oversight and reviewed at the local, national, and international levels. She wanted to bring these efforts to the attention of the working group and suggested that it examine their recommendations.

Malcolm Dando
University of Bradford, U.K.

Dr. Dando stated that in December of 2005, the state parties to the Biological and Toxic Weapons Convention would be meeting to consider the work of the experts group that met in July concerning codes of conduct for the life sciences. He said there is a very strong possibility

that there will be agreement that codes of conduct for the life sciences are important and useful. He hoped that work on this issue by the state parties would be reported to the 2006 Sixth Review Conference of Biological and Toxic Weapons Convention. Dr. Dando stated that if those two agreements go through, NSABB will have had a year to work on the areas they are charged with and will be able to report on progress. He said he believed that the Board's recommendations would be very well received and he wished them well.

The public session was recessed. The Board then met in a closed session.

Adjourn for the Day

Following the closed session, there were no further public comments and the Board adjourned.

I hereby acknowledge that, to the best of my knowledge, the foregoing Minutes and Attachments are accurate and complete.

These minutes will be formally considered by the NSABB at a subsequent meeting; any corrections or notations will be incorporated in the minutes after the meeting.

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Amy P. Patterson, M.D. Date
Executive Director, NSABB and
Director, OBA, NIH

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Dennis L. Kasper, M.D. Date
NSABB Chair