DEPARTMENT OF HEALTH AND HUMAN SERVICES

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NATIONAL SCIENCE ADVISORY BOARD FOR BIOSECURITY

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INAUGURAL MEETING

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THURSDAY,
JUNE 30, 2005

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The meeting convened in the Crystal Ballroom of the Hyatt Regency Bethesda, 7400 Wisconsin Avenue, Bethesda, Maryland, at 8:00 a.m., Dr. Dennis L. Kasper, M.D., Chairperson, presiding.

MEMBERS PRESENT:

DENNIS L. KASPER, M.D.	Chair
ARTURO CASADEVALL, M.D., Ph.D.	Member
MURRAY L. COHEN, Ph.D., M.P.H., C.I.H.	Member
LYNN W. ENQUIST, Ph.D.	Member
BARRY J. ERLICK, Ph.D.	Member
DAVID R. FRANZ, DVM, Ph.D.	Member
GENERAL JOHN A. GORDON (Ret.)	Member

MICHAEL J. IMPERIALE , Ph.D. Member

MEMBERS PRESENT (Continued):

PAUL S. KEIM, Ph.D. Member

STANLEY M. LEMON, M.D. Member

STUART B. LEVY, M.D. Member

JOHN R. LUMPKIN, M.D., M.P.H. Member

ADEL A.F. MAHMOUD, M.D., Ph.D. Member

MARK W. NANCE, J.D. Member

MICHAEL T. OSTERHOLM, Ph.D., M.P.H. Member

DAVID A. RELMAN, M.D. Member

JAMES A. ROTH, DVM, Ph.D. Member

HARVEY RUBIN, M.D., Ph.D. Member

ANDREW A. SORENSEN, Ph.D. Member

ADMIRAL WILLIAM O. STUDEMAN (Ret.) Member

DIANE W. WARA, M.D. Member

EX OFFICIO AGENCY REPRESENTATIVES:

NATALIA COMELLA, Department of State, for John Turner

BRENDA A. CUCCHERINI, Ph.D., M.P.H., Department of Veterans Affairs

ANTHONY S. FAUCI, M.D., NIH National Institute of Allergy and Infectious Diseases

EX OFFICIO AGENCY REPRESENTATIVES (Continued):

MARYANNA HENKHART, Ph.D., National Science Foundation, for Mary Clutter

PETER R. JUTRO, Ph.D., Environmental Protection Agency

RICK KEARNEY, U.S. Geological Survey, for Sue Haseltine

LAWRENCE D. KERR, Ph.D., Executive Office of the President

DALE E. KLEIN, Ph.D., P.E., Department of Defense

TERRY L. LOMAX, Ph.D., National Aeronautic and Space Administration

BORIS D. LUSHNIAK, M.D., M.P.H., Food and Drug Administration, Department of Health and Human Services

JANET K.A. NICHOLSON, Ph.D., Centers for Disease Control and Prevention, Department of Health and Human Services

STUART L. NIGHTINGALE, M.D., Department of Health and Human Services

GERALD PARKER, Department of Homeland Security, for Elizabeth George

CAIRD E. REXROAD, JR., Ph.D., U.S. Department of Agriculture

SCOTT STEELE, Ph.D., Department of Justice

EX OFFICIO AGENCY REPRESENTATIVES (Continued):

DAVID G. THOMASSEN, Ph.D., Department of Energy

JOHN F. TURNER, Department of State

VINCENT L. VILKER, Ph.D., Department of Commerce

RONALD A. WALTERS, Ph.D., Intelligence Community

ALSO PRESENT:

THOMAS HOLOHAN, M.D., NSABB Executive Director, NIH Office of Biotechnology Activities

AMY PATTERSON, M.D., Director, NIH Office of Biotechnology Activities

ELIAS ZERHOUNI, M.D., Director, National Institutes of Health

SPEAKERS AND PANELISTS:

RONALD M. ATLAS, Ph.D., Center for the Deterrence of Biowarfare and Bioterrorism, University of Louisville

THOMAS BOWLES, Ph.D., Chief Science Officer, Los Alamos National Laboratory

PHIL CAMPBELL, Ph.D., Editor-in-Chief, Nature

SPEAKERS AND PANELISTS (Continued):

JUDITH V. REPPY, Ph.D., Associate Director, Peace Studies Program, Cornell University

RAJEEV VENKAYYA, M.D., Special Assistant to the President and Senior Director for Biological and Chemical Defense, White House Homeland Security Council

WENDY D. WHITE, Director, Board on International Scientific Organizations, The National Academies

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P R O C E E D I N G S

(8:05 a.m.)

CHAIRPERSON KASPER: Good morning. My name is Dennis Kasper, and I'm the Chair of this committee.

I'd like to welcome you all to the first meeting of the National Science Advisory Board for Biosecurity, and Dr. Elias Zerhouni will give some opening remarks. Dr. Zerhouni.

DR. ZERHOUNI: Thank you, Dennis. I appreciate it.

Good morning, everybody. I'm Elias Zerhouni, the Director of the National Institutes of Health, and I'm really pleased to be here today to launch what I think is a key component of the administration's biosecurity initiatives in the life sciences.

As you know, the U.S. government created the board to provide advice, guidance, and leadership regarding biological research that has the potential for misuse and could pose a biological threat to the public health or national security. Clearly, this is

an issue that is novel in the field of science, in biology, in particular, in the life sciences, in particular, where dual use is of concern both from the standpoint of biosecurity, but also from the standpoint of free dissemination of useful information to the public.

I had the privilege of being involved in the establishment of the NSABB and the many trans-government discussions that preceded the government-wide collaboration to establish the Board. And I am really pleased to be here to help launch the work of this very important committee.

I think you members of this committee know that the benefits of scientific discovery and innovation, of global collaboration, of the exchange of ideas across borders are endless, and if you look at the international scientific community's rapid efforts to identify and sequence the SARS pathogen in less than a month, it was in record time, using all of the available technologies known to all of us and sharing across borders the knowledge that was being acquired partly in China, partly at the World Health

Organization, CDC, NIH.

We can see the power of the ability to disseminate relevant information on a timely basis. There's no doubt that the dissemination of information and biosecurity measures for controlling avian influenza among poultry flocks today is another example of why we need free, rapid dissemination of information so we can act on it.

The collaboration, for example, that enabled the polymerase chain reaction to identify the fungal infection soybean rust in soybean crops is another example where there is a public good that was achieved.

Or the international efforts that led to the sequencing of the human genome, there's no doubt that scientific advances stem from this long-term and sustained investment in basic and applied research across many government agencies, from the free exchange of scientific ideas, and across the world.

Research programs are aimed primarily at extending our knowledge of the human body and the multitude of organisms with which humans interact and

depend, and from this research, we can gain all the tools, diagnostic and therapeutic tools, that we may need.

So how does the NSABB fit into this picture, and why is it being established now?

I think there is no doubt that our progress in fundamental science for the benefit of mankind has also created tools that have incredible capabilities for mischief. Because of the advances in recombinant DNA research, in molecular biology, genetics, and other life science disciplines, we have come to the root, the real root, of life systems and biological systems. And there is no doubt that over the past 30 years, from the day recombinant DNA technology became available to us; concerns have been expressed about the potential misuse of these technologies.

And as we go forward, we have an increasing ability to routinely alter biological systems, obviously to explore the molecular mechanisms of human, animal, and plant health and disease. Yet it is an unfortunate fact of life that there could be

individuals out there who would use these very technologies and discoveries towards more sinister ends to terrorize nations and threaten public health.

Accordingly, despite the admirable goals and intentions underlying life sciences research conducted to enhance the quality of lives, concerns have been raised that this information could also be misused, and because of that, the Department of Health and Human Services and the National Institutes of Health were asked to be the home for this committee.

We have greatly expanded our biodefense programs as well at NIH to be able to develop the countermeasures necessary against bioterrorism. But at the same time, this threat could not be tackled unless we had a complete engagement of all the components of society that are necessary to provide the wisdom for the country and that will be necessary for us to find the very subtle borders between good use and misuse of these technologies.

I think there's no doubt that the spectrum of responses that one could adopt in the context of threats like this has to be carefully measured. Our

response to these threats must be doing more good than harm. Response to these threats has the potential of doing more harm than good. And our nation's response, we stress, is necessarily a response that has to be coordinated and measured, but also enlightened by evidence, provided through the common wisdom of groups of citizens like yourself with the expertise and with the common sense that needs to be brought in to provide guidance to the rest of the country in the context of providing a safe harbor for good research and an unsafe harbor for research practices that may, in fact, threaten us.

So the term "dual use research" has been coined to refer to this biological research that has legitimate scientific purpose but may be misused to pose a threat to public health and our national security.

That concept could apply to many types of other research, but the specific criteria for identifying dual use research are yet to be defined, and we're counting on you to help us do that, and this is clearly one of the first issues that the Board will

have to consider.

It is important to bear in mind that scientific intent distinguishes dual use research from other types of research that can be used for malevolent purposes. The objective of dual use research is to benefit life and human health, and the work is undertaken for legitimate scientific purposes rather than deliberately caused damage.

The creation of this Board is a government-wide effort to address this very significant and important biosecurity concern in the life sciences. This will be a significant challenge for you, members of the committee. I think many of the decisions you will make will be very public. I think the rationale and the process by which you reach those decisions will be scrutinized as much as the decisions themselves.

We want to adopt a very open and public process to the extent that we can without jeopardizing security. Because it is the sharing of information, materials and technologies that has been the foundation for progress in the life sciences, notably

the participating departments and agencies that are involved in such activities are all committed to striking a balance between the needs of scientific progress and biosecurity, and this balance is reflected in the fact that the Board has been charged with recommending a set of guidelines and with promoting a culture of responsibility.

Let me stop here because there is no set of guidelines that you could develop that will be successful at the end of the day. A culture of responsibility is not established worldwide across the community of scientists. Because at the end of the day, it is my personal belief that the goal will be achieved when a scientist himself or herself asks themselves a question: could this be misused? What do I need to do to protect that from happening?

That culture of responsibility is probably the most difficult task all of us as leaders of agencies, and all of you as members of this committee are going to have to develop and find a way to get to.

This is why I was talking to Dr. Kasper before the opening of the session, and I mentioned to

him the fact that communications from this Board to the scientific community are going to be an important component, and the strategy for communicating, and the strategy for involving the leaders and the opinion makers in science across the world is something that we'd like to hear from you about, and we're very prepared; as the Director of this agency, we're very prepared to support, in fact, the establishment of such a culture, a very difficult task.

There is no doubt that existing laws and regulations are already in place that speak to critical aspects of biosecurity for a particular subset of research involving Select Agents. And these have been enacted already, and these have for intent the purpose of protecting the American public from the misuse of these agents through acts of terrorism.

And in doing so, we have created a framework of laws. The U.S.A. Patriot Act of 2001 was the first one to address the use of certain highly pathogenic biological agents by lab workers and specifies who should be restricted from working with these Select Agents.

I think the Act also establishes personal liability in certain cases for scientists engaged in Select Agent work. I think it's clear that the government is using the means that it has through legislation to limit the risk of biosecurity, of the direct use of a biosecurity threat.

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 and the Agricultural Bioterrorism Protection Act of 2002 updated the existing Select Agent rule by requiring research facilities to register with CDC or USDA if they possess, use or transfer Select Agents on the list of Select Agents.

In addition, the Select Agent rules require the development and implementation of safety and security plans for institutions that work with Select Agents. There's no doubt that these can help address the critical physical biosecurity aspects associated with certain pathogenic organisms while still allowing the development of critical diagnostic tools, medicines, and vaccines.

But this is not enough. Protecting our

nation is going to have to be, in the context of biosecurity, is going to have to be an ongoing and dynamic process.

And I'd like to remind everyone that the Recombinant DNA Advisory Committee of the NIH established many, many years ago went through a similar process of adaptation and evolution, and I think this is why I think this Board needs to really look at its work as a never finished work. Conditions will change. Evolution will be necessary, and hopefully you will evolve guidelines and rules and a new culture of security faster than those who want to misuse dual use research can evolve.

This is really the challenge. Rigidity is probably not the best answer, but clearly, evidence based, wisdom based, aggressive approaches to this issue is something we need from you, and your advice at this meeting, at these meetings is going to be listened to. It will be critical.

Today's inaugural meeting will definitely help strengthen our national biosecurity while fostering essential life sciences. Your charge, as

established, is to specifically advise the government on this critical issue and to recommend strategies for the efficient and effective oversight of federally conducted or supported dual use biological research, taking into consideration both national security concerns, and the needs of the research community.

This is your official charge, ladies and gentlemen.

The new policies and oversight practices that result from the recommendations of the NSABB will complement the existing critical biosecurity initiatives and legislative framework I mentioned.

I want to, first of all, thank all of you who participated in the conceptualization and formation of the NSABB. I see many colleagues from various government agencies, departments, and I want to thank them because this was not an easy task to come up with a recommendation for the president to follow.

And I could like to commend the expert members and ex officio members of the Board for agreeing to serve on the NSABB. You have all been

appointed to this important committee because of your nationally recognized expertise in your field and in your analytical and problem solving abilities. Dual use dilemma is a dilemma. It is a public policy challenge, and it is of extraordinary importance for our society.

And we need your wisdom. We need your good judgment. We need your help, and we need to find the right balance, in a multi-parametric dimensional problem because it is not just a scientific problem, and this is one of the most difficult things we will have to do, being not only scientists, but being citizens of our great country.

So I would like to ask you at this point to stand up and look towards me. I'm going to swear in all of the members. You have received your charge, and if you can just look towards me and stand up, I'd like to ask all of you to raise your right hand and repeat after me:

I do solemnly swear that I will support and defend the Constitution of the United States against all enemies, foreign and domestic. I will

bear true faith and allegiance to the same, that I take this obligation freely, without any mental reservation or purpose of evasion, and I will well and faithfully discharge the duties of the office upon which I'm about to enter.

Thank you very much for your willingness to serve the country. To all of you I would like to bring the thanks of the Secretary of Health and Human Services, the President, and all of the agencies and departments of the government, and to thank you for your willingness to serve the American people.

I really look forward to your deliberations today and tomorrow and really look forward to receiving your reports and recommendations in the future. As Director of the NIH, I can tell you that everything you will communicate to me will be taken extremely seriously. We will diffuse that, those guidelines and that information as effectively as we can throughout the relevant entities of our government and our stakeholders.

If you look at the world of science, you realize that it is also a global world, and clearly,

we will need to hear from you to be able to play our role in the international scene.

We at NIH are proud to serve as the home of the NSABB, and we clearly are looking forward to serving you and supporting you in your very, very important deliberations. I was talking to the NSABB Chair, Dr. Dennis Kasper, and I know he's ready. He's already identified some of the hot topics, including the ones that showed up in the press recently, and I know that Dennis will be a great, able leader.

And I will now have him go into more details about the meeting agenda and for the next two days provide an overview of the responsibility of the Board members.

Dennis, thank you very much.

CHAIRPERSON KASPER: Well, Dr. Zerhouni, thank you very much for starting this meeting and giving the charge to the committee. On behalf of the committee, I will say that we accept your charge. I think it's a very significant challenge that we have ahead of us, but I think that my colleagues are up to the task, and we're all willing to put in the work and

effort that's needed to help define what needs to be defined for the area of biosecurity.

I'd like to just start with introducing myself just briefly, and then in a little while I'll ask all of my colleagues to introduce themselves.

I'm professor of medicine and microbiology and molecular genetics at Harvard Medical School. I'm the Director of the Channing Laboratory at Brigham and Women's Hospital in Boston, and I'm also the Director of the New England Regional Center for Excellence in Biodefense and Emerging Infectious Diseases.

My research interests are in microbial immunity. I have a specific expertise in carbohydrates, and I have a longstanding interest in vaccines, particularly glycoconjugate vaccines and immunomodulation.

The organisms I work with are Group B Streptococcus, anaerobes, such as Bacteroides, and more recently with the organism Francisella tularensis, one of the agents of potential bioterrorism.

So that just gives you a little insight

into what my scientific expertise is about.

I'd like to welcome the Board members, the ex officios, the public in attendance, as well as those watching the proceedings by Webcast.

I just want to go through some of the logistics that will occur over the next two days because there will be presentations on issues that some of us may have considered in great depth; yet for many others, these will be completely new topics.

We'll hear from speakers who represent a broad range of expertise from academia to biotechnology industry, the scientific publishing industry, and the government on issues of biosecurity and public health.

The varying perspectives of the speakers, as well as those of the Board members serve as a great resource from which we will all undoubtedly benefit.

I'd like to give a brief overview of the agenda of the meeting. Board members should refer to the agenda in your table folders. Today we will first hear about the National Science Advisory Board for Biosecurity, purpose, structure and operations.

Subsequently, each member will have an opportunity to briefly express their view on biosecurity in the life sciences.

This afternoon we will have a session on the development of criteria for identifying dual use research and research results. This will be followed by Dr. Anthony Fauci speaking on balancing biosecurity and scientific progress, the need for a culture of responsibility.

The second session for this afternoon will be communication of dual use research results, methods, and technologies.

When we meet tomorrow, we will hear from speakers on the topics of codes of conduct in the life sciences, international perspectives on dual use research, and the chemical synthesis of bacterial and viral genomes.

Following each session there will be a general discussion and question period for Board members and speakers. Throughout the meeting I think we'll all need to bear in mind that a given topic or term may have a different meaning to another

individual based on their experience and point of view. A typical example is the term "dual use," which we are going to learn has many meanings depending on your line of work and the mission of your organization. Coming to common ground on this very concept is of primary importance to NSABB.

At the end of each day, we will conclude with an opportunity for public comment. In order to provide public comment, you must have notified the NSABB staff in advance or, if time permits, we will allow those who have not registered to make a statement.

If you have not already registered and would like to give public comment, please contact a staff member at the registration table.

My role as chair is to oversee the NSABB and the conduct of our meetings. The NSABB has been charged to advise, recommend on policy relevant to particular issues related to biosecurity and public health. We will hold regularly scheduled meetings. However, the Secretary of the U.S. Department of Health and Human Services, Mr. Mike Leavitt, has also

asked us to convene special sessions if occasions arise that would require NSABB deliberations and guidance.

We have a significant set of tasks in front of us. In order to facilitate our work and address current topics in a timely manner, we will be forming working groups that will have specific areas of focus. These will include groups on dual use research, communications, codes of conduct, international collaboration, and synthetic genomics. These groups will be composed of regular and ex officio Board members, as well as outside experts. The groups are expected to confer between our regularly scheduled meetings and to develop draft work products for the Board, such as position papers in collaboration with NSABB staff working at the NIH.

They will present their recommendations to the entire Board. It will be the entire Board that decides on any products that will be put forward to Secretary Leavitt and his colleagues in other federal departments and agencies.

It's important to emphasize that the

entire Board will be involved in every decision, the entire Board. As we begin exploring the issues charged to the Board, I'd like to ask the members to begin thinking about the working group in which you would like to participate.

We will return to the task of forming the groups as part of our closing session tomorrow.

Before the Board members introduce themselves, please be aware that there are 45 minutes for introductions, and we have 43 members. So let's take a minute or so to introduce ourselves, our fields of interest, experience serving on other federal advisory committees, et cetera.

Please keep in mind that the session in which we will have an opportunity to express our perspectives on biosecurity and the life sciences is coming up later in the agenda, and we can reserve discussion of these issues until then.

Three Board members could not be with us today. They are Anne Vidaver, Professor and Chair, Department of Plant Pathology, University of Nebraska. She'll be with us tomorrow.

Dr. Claire Fraser, President and Director of the Institute for Genomic Research.

And Dr. Tom Shenk, Professor in Life Sciences, Department of Microbiology at Princeton.

The speakers this morning reinforce the fact that much was expended of effort to select Board members with a broad spectrum of knowledge and proficiencies. As each Board member briefly introduces themselves, you will note the depth of expertise and breadth of perspective represented on NSABB.

I'd like the ex officios to mention how the interest of their respective departments coordinate with NSABB.

Later today, I will need to leave the meeting temporarily. In my absence Dr. Paul Keim has graciously agreed to serve as pro temp chair.

So we will begin the introduction with Dr. Keim and work our way around the table. Paul.

DR. KEIM: Thank you, Dr. Kasper.

I am Paul Keim. I'm the Director of Pathogen Genomics at the Translational Research

Institute in Phoenix, Arizona. I also hold the Cowden Endowed Chair in Microbiology at Northern Arizona University. So I work in both a research institute as well as in academia.

My research interests have been in genomics for a very long time and how you detect variation in genomes and how you translate that into diagnostics and into forensic analysis. My laboratory has been actively involved in investigating the anthrax letter attacks and, in fact, still does today.

We face the question of dual use on a regular basis in my laboratory and have to make decisions both in the laboratory concerning what we do. We have to base decisions on when we publish and how we publish. At the same time, how do we move the science forward in order to help this country?

So I'm looking forward to this opportunity to work through these issues in the next coming years.

Thank you.

DR. ROTH: I'm Jim Roth. I'm a veterinarian and a professor of immunology at Iowa State University, College of Veterinary Medicine. My

area of expertise is infectious diseases of cattle and swine, and the first 20 years of my career, I worked on domestic diseases and in the last four or five years, I've been very interested in vaccine for foreign animal diseases, which are a huge threat to both public health and food security in the U.S.

I'm director of the Center for Food Security and Public Health, which is a CDC specialty center in veterinary medicine and zoonotic diseases. I also served on the White House Office of Science and Technology Policy Blue Ribbon Panel on Agriterrorism Countermeasures and chaired the vaccine subcommittee.

DR. OSTERHOLM: I'm Mike Osterholm. I'm the Director of the Center for Infectious Disease Research and Policy at the University of Minnesota, as well as the Associate Director of the National Center for Food Protection and Defense, at the DHS Center of Excellence and also at the University of Minnesota. I have been there since 2001.

Prior to that time, I was at the Minnesota Department of Health and served as the State Epidemiologist for 25 years.

In addition to that, I also have served as a special advisor to Secretary Tommy Thompson from 2001 to 2004 in the areas of bioterrorism.

My background is basic infectious disease epidemiology and public health preparedness, and I've been involved in the area of bioterrorism dating back to the early 1990's.

DR. LUMPKIN: I'm John Lumpkin. I'm Senior Vice President of the Robert Wood Johnson Foundation. Prior to coming to the Foundation, I was Director of Public Health in the State of Illinois for almost 13 years, and before that I practiced as an emergency physician.

Prior to or actually up until January, I also chaired the National Committee for Vital and Health Statistics, Advisory Committee to the Secretary on Health Information Policy.

DR. LEVY: My name is Stuart Levy, and I am currently Professor of Molecular Biology, Microbiology, and of Medicine at Tufts University, School of Medicine, and I direct the Center for Adaptation Genetics and Drug Resistance.

My main interest has been antibiotic resistance, a field that I've been interested in for about 30 years. I co-founded the Alliance for Prudent Use of Antibiotics. My work is both bench science and public health. I've served as a consultant to the World Health Organization, the FDA, and many other government agencies, including NIH, and I'm pleased to be here.

DR. FRANZ: My name is Dave Franz. I'm the Senior Biological Scientist at the Midwest Research Institute in Kansas City, and also serve as the Director of the National Agricultural Biosecurity Center in Kansas State University.

I had an Army career for 27 years. The last 11 of that were at Fort Detrick at the U.S. Army Medical Research Institute of Infectious Disease, and I did serve on the Fink Committee that was involved in the developments that led to this committee.

DR. ERLICK: My name is Barry Erlick. I have a consulting group. I'm president of BJE Associates. Prior to that I was advisor to the Deputy Secretary, Secretary of Agriculture for Biosecurity.

Previously I have spent 25 years in the intelligence community dealing with specifically dual use issues, primarily in the biological area, and this has been a major concern for a quarter of a century at least for me and even longer.

My background essentially is molecular biology and virology, and I hope to bring some of this expertise to the group.

Thank you.

AMD. STUDEMAN: My name is Admiral Bill Studeman, U.S. Navy, retired. I'm also retired Vice President of Northrop Grumman, and I'm a career "spook."

My government positions included Deputy Director of Central Intelligence, Director of the National Security Agency, Director of Naval Intelligence, and some other positions.

I'm a member of the Defense Science Board, and I just recently completed 15 months being a commissioner on the Presidential Commission on WMD.

My concerns have to do with optimizing the intelligence community's role, particularly in this

period of transformation for the intel community, and including the new Office of the Director of National Intelligence, in terms of how the intelligence community plays its role in biosecurity.

DR. KEARNEY: Mr. Chair, shall we continue with the other Board members before we move to the ex officio members?

DR. WARA: I'm Diane Wara. I'm a Professor of Pediatrics at UCSF, the Director of the Children's Clinical Research Center there, and the Division Chief of Pediatric Immunology.

My research interests are in pediatric HIV, specifically transmission of HIV and strategies to prevent transmission, as well as defining the pathogenesis of primary immunodeficiency disorders for rare groups of congenital diseases, and strategies for reconstitution of these disorders.

I'm currently the chair of the Recombinant DNA Advisory Committee, and I'm here to represent that committee and to act as a continuum between NSABB and the RAC.

DR. RUBIN: I'm Harvey Rubin. I'm a

Professor of Medicine and Microbiology, Biochemistry, and Computer Science at the University of Pennsylvania. I'm the Director of Penn's Institute for Strategic Threat Analysis and Response, which is a 12-school consortium of faculty and students doing research in everything from risk analysis to robotics and how that plays into security and strategy issues.

My research interests are in biochemical reaction mechanisms of enzymes that are in Mycobacterium tuberculosis, with the multi-drug resistant items in Category C bioagent, and we're interested in how biochemical and genetic switches get turned on and off as Mycobacterium tuberculosis goes through its various life cycles in dormancy and activation.

DR. IMPERIALE: My name is Mike Imperiale. I'm a Professor of Microbiology and Immunology at the University of Michigan Medical School.

My research interests are in DNA tumor viruses and in viral life cycles and how they contribute to cancer, and more recently we've moved into the field of using viruses for gene delivery and

also as recombinant vaccines, and I currently sit on the National Gene Vector Laboratory Steering Committee.

I'm also the chair of the Institutional Biosafety Committee at the University of Michigan, and so between my own research and serving on that committee, I get to see a lot of different manipulations to various viruses and bacteria, and I hope to be able to contribute to this committee through those efforts.

DR. RELMAN: I'm David Relman, Associate Professor of Medicine and Microbiology at Stanford University. I'm also an infectious disease clinician and Chair of the Stanford Administrative Panel on Biosafety.

My research interests have to do with the microbial ecology of the human body, as well as pathogen diversity, pathogen detection, and the genomic aspects of host-microbe interactions.

My service and interests in the areas of dual use and biosecurity involve a variety of advisory functions to the U.S. government, various agencies

having to do with the potential developments in biotechnology that are relevant to threats to health and misuse, and I currently co-chair a committee at the National Academy of Sciences with another committee member, Stan Lemon. This committee is charged with a look at the future of biotechnology and its potential impact on biological security, misuse of biology, et cetera. So these are issues that are relevant to this committee as well.

MR. NANCE: My name is Mark Nance. I'm an attorney in private practice, corporate and intellectual property law with a focus on biotechnology. I am currently the senior counsel, Discovery Systems, for G.E. Health Care.

Prior to that I was affiliated with a company focused on the environmental and IDD nucleic acid based detection of biowarfare agents.

DR. MAHMOUD: I'm Adel Mahmoud. I'm a physician in infectious diseases, specialist. I run vaccines at Merck and Company, Inc. We have several vaccines that translate most of the findings of basic research into agents that we use to protect our people

in this country and locally.

My interest in the area relates to 25 years previously in academic medicine and on the host-pathogen relationship.

DR. LEMON: I'm Stan Lemon, a physician trained in infectious diseases, currently a Professor of Microbiology and Immunology in internal medicine at the University of Texas Medical Branch in Galveston, where I direct the UTMB's Institute for Human Infections and Immunity.

The institute manages the containment laboratories that do infectious disease research at UTMB. That includes quite a bit of BSL-3 and functional BSL-4 space.

I also serve as principal investigator for the Galveston National Laboratory, one of two national biocontainment laboratories under construction with funding from the National Institutes of Health.

I co-chair with David Relman the IOM NRC committee that he mentioned just a moment ago, and also serve as vice chair for the Forum on Microbial Threats at the Institute of Medicine.

GEN GORDON: I'm General John Gordon, retired Air Force. My friend Bill Studeman is a career spook. I'm probably the career policy wonk that shows up in this business. I spent 32 years in the Air Force and mostly in strategic systems, you know, arms control, nonproliferation, and my last job was as Deputy Director of Central Intelligence, a couple of years at the Department of Energy, the National Security Administration. My last two jobs in government were Chief of Counterterrorism in the White House and then the President's Homeland Security Advisor for a year.

I first became interested and involved in this subject primarily as a result of the Fink Commission also, and helped to bring that report into the White House and get some light on it.

Thank you.

DR. ENQUIST: My name is Lynn Enquist. I'm the Chairman of the Department of Molecular Biology at Princeton University. I'm the past President of the American Society of Virology. I'm a board member of the AAAS, and I'm the Editor-in-Chief

of the Journal of Virology.

My career focuses predominantly on running a laboratory to study the pathogenesis of herpes viruses that infect the nervous system. I have spent my career in at least three different areas. I worked as a staff scientist at the NIH in the early 1970s developing a lot of the methods for recombinant DNA technology and using them.

I was Research Director of a small biotech company to develop animal virus vaccines. I was a research leader at DuPont in corporate research, and then a Senior Research Fellow at DuPont Merck before I went to Princeton to run an academic laboratory.

One of the things that I'm really quite proud of and the reason why I'm quite interested in the issues at stake here is that at the American Society for Microbiology, the Journal of Virology is one of 11 journals, and about four years ago we decided as a group to instill a culture of responsibility in our membership to publish, and I'll be talking a little bit more about what we've done.

The Journal of Virology, for example,

we've looked at over 16,000 manuscripts in the last four years, and with the light of understanding the kind of science that's there, and I'll be telling you more about that as we move along.

DR. COHEN: Good morning. I'm Murray Cohen, retired Public Health Service officer currently based down in Atlanta. I serve as independent consultant, but also as President of the Front Line Health Care Workers Safety Foundation, public, not-for-profit, engaged in training first responders and first receivers in matters of disaster management, mass casualty management and that sort of thing.

Currently I'm very involved globally in risk assessments and threat assessments for high containment laboratories. I'm very involved with and concerned about training people appropriately to work in these laboratories and manage these laboratories effectively and safely.

DR. SORENSEN: I'm Andrew Sorensen, Professor of Epidemiology and President of the University of South Carolina. I previously served as Executive Director of the AIDS Institute at Johns

Hopkins Medical Institutions, and since its inception served as a member of the DHHS Secretary's Council on Public Health Preparedness and Bioterrorism.

DR. REXROAD: I'm Caird Rexroad. I represent the USDA as an ex officio member. I am the Associate Administrator of the Agricultural Research Service and in charge of program planning.

My background is as a scientist trained as a reproductive biologist with most of my career spent working on transgenic animals, insertion of genes to modify or protect animals against various infectious diseases.

Today we're very interested in the activities of this committee because of the tremendous drive that genomics has brought to the kinds of research. USDA sponsors over $1.5 billion worth of biologically based research, and with the tremendous increase in emphasis on countermeasures against various threat agents, we see the likelihood that we will be involved in some areas of very sensitive research and look forward to the advice from this committee.

DR. HENKART: I'm Maryanna Henkart. I am representing the National Science Foundation on behalf of Mary Clutter, who is the Assistant Director of the National Science Foundation for the Biological Sciences.

I am the Director of the Division of Molecular and Cellular Biosciences, which means that I oversee programs in the traditional disciplinary areas of biochemistry, biophysics, cell biology and genetics and genomics. I also oversee programs in microbial genome sequencing and a program we have called microbial observatories, both of which we are doing in collaboration with the Department of Agriculture.

We have another program that I oversee which is called the Ecology of Infectious Diseases. Obviously, the National Science Foundation's primary mission is to see to the long-term welfare of fundamental science and engineering research and education in this country, and we are very concerned about the role of fundamental science and the impact of fundamental science on biosafety and the impact of biosafety activities on fundamental science.

DR. LOMAX: I'm Terry Lomax. I'm Deputy Associate Administrator for Research at NASA, and I'm part of the Exploration Systems Mission Directorate. We have the responsibility for all of the human biological space research at NASA.

And I'm on loan from my home institution, which is Oregon State University, where I'm Professor of Biotechnology and Gene Research, and prior to coming to D.C., I was Director of the Program for the analysis of biotechnology issues.

DR. WALTERS: I'm Ron Walters. I am a molecular biologist. I currently work in the Intelligence Technology Innovation Center that is in the Office of the Director of National Intelligence.

I represent the intelligence community and the programs on which we work are countering biowarfare and bioterrorism.

DR. KERR: Good morning. I'm Larry Kerr, Assistant Director for Homeland Security in the Office of Science and Technology Policy at the White House. I'm a molecular immunologist by training, and our office is engaged in a wide variety of activities that

facilitate the coordination of the federal agencies across a multitude of Homeland Security science and technology issues.

DR. JUTRO: Good morning. I'm Peter Jutro. I'm Deputy Director and Chief Scientist of EPA's National Homeland Security Research Center, an agency that has responsibilities in drinking water protection, decontamination and risk.

My academic training is in biology and mathematics with work in risk assessment, chemical ecology, and infectious disease. I serve on the Science Advisory Boards of several other parts of the government, especially in the intelligence community.

I'm in an agency with a 30 to 40-year commitment to open science and sharing information with the public, in fact, one with a legal mandate to do so, yet my center regularly faces dual use and sensitive information release issues. Our mission is to protect the public, but our research work is often a road map to efficient terrorist action. So we are very interested in the advice that we can glean from the work of this committee.

DR. CUCCHERINI: I'm Brenda Cuccherini, from the Department of Veterans Affairs, Office of Research and Development. My primary areas there are in policy development related to biosafety, biosecurity, our BSL-3 program, and our Select Agent use.

I also develop policies in the areas related to human subjects research and conflict of interest, and I serve on a number of interagency committees and subcommittees on biosecurity.

My background is in occupational and environmental health.

MR. TURNER: Good morning. My name is John Turner. I'm an Assistant Secretary at the U.S. State Department. I oversee the International Health Office, which has responsibility over infectious diseases other than HIV, malaria and TB. We also have oversight over environmental health, and I represent the Secretary on biosecurity issues.

We also have the international lead on science and technology agreements out around the world, and forge some of our sustainable development

strategies dealing with access to sanitation and hygiene in dealing with waterborne diseases.

My background is life sciences and wildlife ecology, although I have to admit that those scientific credentials wandered off campus probably years ago.

Thank you.

DR. STEELE: Good morning. My name is Scott Steele representing the FBI. My background previously was in genetics. I completed my Ph.D. at Princeton and from there moved on to study issues of science, policy and security, particularly increasing outreach between the scientific and security communities.

At the FBI I'm focused on working on a number of WMD countermeasures programs, particularly working with other federal departments and agencies to examine programs for surveillance, detection, and response to the threat of WMD and several biodefense initiatives, including the one that led to the creation of the NSABB.

Thank you.

MR. KEARNEY: My name is Rick Kearney. I'm a wildlife biologist. I'm here representing Dr. Susan Haseltine, the Associate Director for Biology within the U.S. Geological Survey in the Department of the Interior.

As the Science Bureau in the Department of the Interior, USGS has responsibility for providing the information necessary to protect the health and welfare of their roughly 20 million visitors to our national parks, wildlife refuges, as well as managing the one-fifth of the U.S. land mass under the Department of the Interior control.

Our interest here today is to increase the linkages between the Native communities, that is, the study of the Native communities and that of human health and agricultural animal communities, and we look forward to advising and learning from this panel.

Thank you.

MR. PARKER: My name is Gerry Parker. I'm with the Department of Homeland Security in the Office of Research and Development in the Science and Technology Directorate. I oversee and manage a broad

array of Homeland Security research and development programs, to include our biocountermeasures programs.

I retired from the Army about a year ago after 26 years, spent a lot of that time in medical biodefense research spanning from vaccine, diagnostic, drugs, and in basic pathophysiologic mechanisms.

Thanks.

DR. NICHOLSON: Good morning. I'm Jan Nicholson. I am the Associate Director for Laboratory Science in the National Center for Infectious Diseases at CDC. The IBC at CDC actually sits in my office. I have represented biosecurity in a variety of forms. Part of my job involves representation of laboratory issues in infectious diseases.

DR. LUSHNIAK: Good morning. My name is Boris Lushniak. I'm a Captain, U.S. Public Health Service, currently serving as the Assistant Commissioner for Counterterrorism Policy at the Food and Drug Administration.

Prior to that I served with the Centers for Disease Control, National Institute for Occupational Safety and Health. I am a medical

officer, physician, Board certified in dermatology, family practice, and preventive medicine.

I represent the FDA here on this panel, and I certainly am looking forward to interacting with this group.

Certainly, FDA's mission which revolves around safety and security aspects for our food supply and the availability of medical countermeasures really depends on research to make progress in this area, and so certainly we seek the advice and guidance from this committee.

Thank you.

DR. DIXON: Good morning. I'm Dennis Dixon, and I'm Chief of the Bacteriology and Mycology Branch at the National Institute of Allergy and Infectious Diseases and have had ongoing responsibilities with Select Agents and a lot of other activities relating to key organisms under discussion here today. I'm very pleased to be here on behalf of Dr. Fauci, who is the Director of the National Institute of Allergy and Infectious Diseases, and will be joining us this afternoon to comment on the

institute's substantial involvement in this area.

DR. THOMASSEN: Good morning. I'm David Thomassen from the Department of Energy. I'm the Chief Scientist for the Office of Biological and Environmental Research.

The two areas that are probably of greatest interest to the Department of Energy with regard to this committee are our efforts to understand, develop comprehensive understanding of nonpathogenic microbes, microbes that could be used to develop biotechnology solutions for energy and environmental issues.

We fund a variety of research ranging from DNA sequencing to technology development, to understand and characterize all of the proteins and regulatory networks and microbes, and also fund some research that we will hear about tomorrow in terms of synthetic genome development. So we're very interested in the deliberations of this committee.

The other area, I think, of interest to the department, which hopefully will get on the agenda of this committee as well, is that of nanotechnology.

DR. KLEIN: My name is Dale Klein. I represent the Department of Defense. I'm currently a presidential appointee in charge of the chemical, nuclear, and biological defense programs of the Department of Defense.

Prior to my appointment, I served as Vice Chancellor of the University of Texas System. I'm on leave from the University of Texas at Austin, and my view of the world has changed somewhat from the role of academia, where we publish everything, to starting my morning with an intel report and looking at those that want to do us harm.

The consequences of a biological attack are very sobering, and it will be a challenge to strike that balance between free flow of information and protecting the nation against those who want to do us harm.

DR. NIGHTINGALE: Good morning. I'm Dr. Stuart Nightingale. I'm the Deputy Assistant Secretary for Public Health Emergency Preparedness in the Office of the Secretary for the Department of Health and Human Services. I'm also the Senior

Medical Advisor to the Director of the Office of Global Health Affairs at DHHS.

I'm an internist, and I've been involved over the years primarily with medical administrative matters in the Food and Drug Administration and the Office of the Secretary, particularly the intersect between medical practice issues and regulatory concerns, and more recently, of course, in the Office of Public Health Emergency Preparedness, the CBRN issues, as well as the manmade or natural, rather, natural disease problems, such as influenza.

Our office is the focal point for the department. We work closely with CDC, FDA, and NIH on these various issues.

I am also the HHS liaison to the Biological Weapons Convention group at the State Department, and work very closely with various parts of the Department with the coordination with the World Health Organization.

And finally, our office has been deeply involved in the translation of the Fink report into this NSABB. So I'm very pleased to be part of this

group.

DR. VILKER: Good morning. My name is Vincent Vilker. I'm representing the Department of Commerce. We have two research agencies within Commerce. One is NOAA, the National Oceanic and Atmospheric Administration, and the second is the one where I come from, the National Institute of Standards and Technology, where I am the Chief of the Biotechnology Division.

Some of the work that my role and that of NIST is measurements and data, validating both, and what we bring to this forum, I think, examples include the reference materials that are used in DNA typing for forensic purposes and also by the Department of Defense for human identification.

In addition, we've developed reference materials in an international forum for benchmarking real time PCR measurements, which I think you might recall Dr. Zerhouni referred to as one of the major technologies used in microbial identification.

So in a nutshell we develop reference materials and validate procedures across a wide

spectrum of technologies, in this case biotechnologies, for the purpose of facilitating commercial application of scientific discovery for establishing societal good.

Thank you.

CHAIRPERSON KASPER: I notice that Dr. Arturo Casadevall joined us. Arturo, would you introduce yourself, please?

DR. CASADEVALL: Arturo Casadevall from the Albert Einstein College of Medicine. I am the Director of the Division of Infectious Diseases, and I am also professor in the Department of Microbiology, Immunology, and the Department of Medicine.

I believe I'm here in this committee because of my expertise in host-microbe interactions.

Thank you.

CHAIRPERSON KASPER: Well, thank you all for those introductions. I'm very pleased that everyone will be able to participate in today's meeting and in future meetings.

Now I'd like to introduce Dr. Thomas Holohan, who is the Executive Director of NSABB, and

he'll give us an introduction to NSABB, its purpose, its structure and operations.

DR. HOLOHAN: Thank you, Dr. Kasper.

And good morning, ladies and gentlemen. I'm pleased to have the opportunity to provide a brief description of the purpose, structure, and function of the National Science Advisory Board for Biosecurity.

This Advisory Board has been established as a result of increasing concern that there exists a risk for the malevolent use of life sciences research and research results and that the strengthening of biosecurity initiatives is a prudent course of action.

Over the last few years, the government has implemented a number of initiatives to address those concerns, as detailed on this slide, and as previously described by Dr. Zerhouni, the Patriot Act of 2001, the Public Health Security and Bioterrorism Preparedness and Response Act, and the companion Agricultural Bioterrorism Protection Act of 2002.

And in addition, government promotion and the conduct of research on the development of countermeasures for biologic threats. The legislation

as Dr. Zerhouni mentioned placed new restrictions on access to certain materials and in some cases imposed criminal penalties.

In the same time frame, the National Research Council produced a report concerning biotechnology research and the potential for that research to be intentionally used for malevolent purposes. This was generally believed to have been a cogent view of an increasingly problematic situation.

The NRC committee employed the term "dual use" for technologies which serve the legitimate scientific purpose and which could be used to improve wellness, but also had the potential for misuse with resultant harm to national security or to public health.

The report specified a number of experiments of concern as archetypes of dual use research.

In addition, it provided a number of recommendations. These included the creation of the National Advisory Board and the report called attention to issues of education of the scientific

community regarding dual use research, review of particular research proposals, date of publication, and communication between groups responsible for health and for security.

As you will see, the charter of this Board is quite comprehensive, reaching all of those recommendations and more.

The National Science Advisory Board for Biosecurity was established to advise the Secretary of the Department of Health and Human Services, the Director of the NIH, and the heads of all federal entities that conduct or support life sciences research to recommend strategies for the effective oversight of federally conducted or supported dual use research, where dual use research as you've already heard and will probably hear again many times over the next two days, is research with a legitimate purpose that may be misused to result in a threat to public health or to national security.

Importantly, the National Science Advisory Board for Biosecurity will consider both the needs of the research community and concerns about national

security.

There are a number of charges to the Board, one general and 11 specific charges. The Board is charged to develop criteria that can be used to identify dual use research and also to develop guidelines that can provide for oversight and monitoring of that research and those research results. These are arguably essential requirements upon which other responsibilities of the Board depend.

The Board is charged to advise on national policies governing local review and approval of dual use research to include guidelines for case-by-case review by institutional biosafety committees.

The Board is also asked to advise on criteria and processes for referral of specific classes or specific experiments from local reviewers to the Board itself. And these include the provision of review or guidance on experiments that may exemplify a significant or a complex permutation of research or a new category of dual use research.

And in addition the Board is charged to provide for a response to a research institution's

request for interpretation or application of the developed guidelines to specific research proposals that have been denied by an institutional biosafety committee.

The Board is also asked to provide recommendations on the development of a code of conduct for scientists and laboratory workers, which is intended for implementation and adoption by professional societies and by institutions engaged in life sciences research.

As well, the Board is charged to recommend on the development of mandatory education and training in biosecurity for those scientists and laboratory workers at federally funded institutions and additionally charged to advise on national policies for publication, communication, and dissemination of methods and the results of dual use research.

The National Science Advisory Board for Biosecurity is charged to recommend strategies for coordinated international oversight of dual use research, and further, the Board is charged to advise on policies for the conduct of dual use research that

allows strategies for allowing rapid scientific progress while assuring national security, a point emphasized by Dr. Zerhouni in his introduction.

Finally there is a general charge for the Board to address other issues as the Secretary of Health and Human Services may direct.

The Board charter calls for not more than 25 voting members who are appointed by the Secretary following consultation with other agencies and departments. The Board will meet quarterly and as needed, determined by the Secretary, and the meetings of the Board will be open to the public unless in certain circumstances otherwise determined by the Secretary of Health and Human Services.

And the Board will be managed and administered by the National Institutes of Health, Office of Biotechnology Activities.

Obviously, I'm not going to read all of the expertise on this slide, but as can readily be seen and as you've heard, this Board is a distinguished group of extensive knowledge, skills and experience. It is of note that these capabilities are

broader than those ordinarily represented on biomedical advisory committees and include individuals with proficiency in areas such as security, intelligence, food production, law, and scientific publishing.

In addition to the voting members, there are 18 ex officio members who represent the federal agencies and departments from which you've just heard. These individuals will assist the Board members by serving as a resource for unique expertise and experience as the Board's deliberations reach to their organization's areas of responsibility.

The Board will engage the biosafety, security, and life sciences research in public communities and the Board's activities, including development of the guidelines, codes of conduct, and the training programs previously mentioned. The Board will recognize and develop strategies to address the significant challenges that will be faced by researchers, institutional biosafety committees, the leadership of institutions, and research administrators, and publishers.

I said that the Board was administered by the National Institutes of Health, Office of Biotechnology Activities, and our assignments really are to manage the NSABB on behalf of the department. We will plan and execute the meetings, develop background materials and provide support for the development of work products of the Board to maintain the Website of the Board as a resource for the public; to identify and analyze dual use research issues which we believe are likely to be a continually moving target; to facilitate coordination in the development of federal policies, regarding dual use research; to participate in the implementation and the interpretation of the guidelines developed secondary to the recommendations of the Board for dual use research; and to develop training and education programs for institutional biosafety committees who are involved in dual use research.

The National Science Advisory Board for Biosecurity has its own Website, and the Website address and E-mail address are listed here, and as I've said, the National Institutes of Health, Office

of Biotechnology activities will provide executive functions for the tasks assigned to the National Science Advisory Board for Biosecurity, and you see here our phone, fax numbers, and our address.

Thank you for your attention, and Dr. Kasper, do you wish to allow the audience to take a break?

CHAIRPERSON KASPER: Well, why don't we see if there are any Board members who have questions for you?

DR. HOLOHAN: Sure.

CHAIRPERSON KASPER: Please feel free to ask questions. It's a large charge we have.

DR. HOLOHAN: Either the presentation was very good or their intrinsic brilliance satisfied them.

CHAIRPERSON KASPER: We'll see.

Why don't we reconvene at 9:45? We're running a little ahead of schedule, and that would give us some extra time for discussion after the break.

Thank you.

(Whereupon, the foregoing matter went off the record at 9:16 a.m. and went back on the record at 9:48 a.m.)

CHAIRPERSON KASPER: Why don't we reconvene the meeting?

So at this time I'd like to give NSABB members and ex officios an opportunity to comment briefly about biosecurity issues in the rapidly evolving areas of life science research.

I'll start by reading a statement from Dr. Anne Vidaver, who as I mentioned earlier will be here tomorrow, and I'm just reading her statement now.

"To paraphrase the wife of a Founding Father of the country, not to forget the ladies in drawing up the Constitution, I would remind people not to forget plants which are the basis of all life on earth. For example, one of the largest crops grown in the U.S. is soybeans. Soybean rust, which just entered the country last year, is expected to be a challenge in management at many levels, including that there are no commercial varieties available with any resistance.

"Communication and interaction between animal and clinical scientists with plant pathologists is highly desirable as more bacterial and fungal pathogens of plants are shown to be cross-infective in animals and people. This becomes even a more serious problem with agents that are or can multiply antibiotic or antifungal resistance."

So that everyone has an opportunity to be heard, I ask that you limit your comment to about three minutes at the most, and I'm going to ask Secretary Turner to start.

MR. TURNER: Well, thank you, Mr. Chairman.

As I said in the introduction, the State Department's role is to work with all of you in facilitating, molding the strategy and implementing it, and I think we all recognize that the purpose for which we're organized here is transnational in its scope, and so if we're going to be successful, we have to transmit a new code of conduct on dual research out into the international community.

And so our goal is to work with all of you

to, first, increase international awareness of the issue and then how do we motivate allies and folks that aren't our allies to work in accordance with what's their best interest and the interest of the American people.

Interesting enough, I was at two forums yesterday which were different but have some of the same related questions. One was a hearing before Chairman Hyde's committee in the House on the impacts of waterborne diseases out around the world, and then in the afternoon, a meeting at the White House as we're trying to mold an international strategy for cooperation engagement as we deal with avian flu, avian influenza.

And some of the questions then that perhaps we would look at are what some of our specific goals internationally might be. What international pathways do we choose to transmit what we develop in this committee, international forums like WHO or FAO and many others, what special groups like the G8 or the Global Health Security Action Group? Some come to mind.

What specific countries would we want to work bilaterally with either countries that are strongly our allies or how do we deal with sensitive states, states that might be high threat to the United States in this arena in the research arena or how do we deal with the states in between?

What's our message to those states, depending on the audience? What resources is the U.S. prepared to share with other countries as we work to protect American citizens and our food supply and our economy and our culture and our social values?

What research would we be interested in collaborating on, especially those very sensitive areas of countermeasures?

So we look forward to working with all of you as we have two offices. One deals directly with infectious diseases, but the other office takes a diplomatic lead on all science and technology agreements out around the world in cooperation with all of you.

So we see the NSABB as an important step forward as we look to enhance cooperation in the

health sciences and, indeed, secure a better and more stable future for American citizens and the global family.

Thank you, Mr. Chairman.

CHAIRPERSON KASPER: Thank you.

I think now we'll turn to the Board members and ask each to give their view of this area.

One issue that has been brought to my attention is that apparently the folks sitting in the back of the room are sometimes having trouble hearing people speak. So can you hear me speak in the back of the room?

Okay. So if you just make sure you talk into the microphone, that would be very helpful, I think.

Paul, do you want to start?

DR. KEIM: I guess I'd just like to remind everybody what we have to lose in this process. You know, the United States scientific community and the European world community has really generated an enormous amount of progress in the last several decades, and this has really been based upon a

competitive and interactive process where information was free to flow not only to your collaborators, but also to your competitors so that any result or any progress that you might make would be instantly peer reviewed and critiqued and vetted in a scientific dog fight, if you will.

In the process of increasing our security, it's going to be necessary to begin restricting certain aspects of this. If we don't do this carefully, we, in fact, run the risk of losing what's really the greatest scientific engine the world has ever seen, and in what really should be viewed as a race as opposed to an all or nothing type situation where we are racing against bioterrorists and against people who are against our society and country.

In a race like this, we have to be careful not to hinder ourselves too much while trying to inhibit them to the maximum amount possible. So how is this going to be done?

Well, in individual cases we won't always be able to say that this absolutely has to be stopped because there will be a risk and a cost to anything

that we do in this arena. So it's important for us to try to do this in a very careful fashion so that we end up maximizing our effort while hindering the opponents as much as possible.

DR. ROTH: Okay. My role on this is, I think, to represent veterinary medicine and the animal aspects of the infectious diseases. If we consider that all of the bioterrorism agents except small pox infect at least some species of animals and the majority infect either the companion animals that live in our home or domestic animals we depend on for food, or the wild animals that are so prevalent, it's a huge task if we have to think about controlling these diseases in animals.

And given that these infections can spread from animals to humans, if we want to control them in humans, we need to control them in animals also or we won't succeed.

In addition, there's a long list of foreign animal diseases that present severe threats to the agricultural economy and the agricultural economy broadly defined is the biggest segment of our economy,

and whether those are accidentally or intentionally introduced, there's an urgent need to develop better diagnostics, vaccines, and other countermeasures to protect our food supply.

If we consider the recent emerging diseases, some recent emerging diseases, BSE or mad cow disease, which emerged in England, West Nile virus which emerged in this country, avian influenza which prior to 1997 was not considered zoonotic and is now considered perhaps the biggest threat for a pandemic; Nipah virus, which was a virus which spread from fruit bats to swine to people in Malaysia.

In every one of those recent examples, far more people died than died in our anthrax bioterrorism event, and the best way in all of those examples to control human infection is to prevent or stamp out the disease in animals.

Given that, there's a very small group of researchers that focus on the animal aspects of these diseases and that are without a lot of funding. So in this race, which is urgent that it be run very rapidly, it's more like the tortoise and the hare with

the tortoise trying to control all of the diseases in many species of animals, many more diseases than just the bioterrorism agents.

So it's imperative that we be able to do that rapidly, but yet safely, and the safety is imperative also. So that in our efforts to do good, we don't end up ultimately having a road map and doing harm to what we're all trying to do.

Thank you.

DR. OSTERHOLM: Thank you, Mr. Chairman.

I would suggest at the outset here that this particular Board is going to be one that is going to be a lot like sailing. We're going to be tacking a lot, and that we will probably find ourselves from time to time realizing we've gotten a little too far over in one direction and coming back to the middle and then maybe moving to the other side.

And I don't think that that should at the outset be interpreted as anything bad because we are feeling our way through a very difficult time.

You know, I look at the issue of biotechnology and where we're at today, and I would

agree wholeheartedly with Dr. Keim's points about progress, but just as there was a great step forward in the warfare world when they went from swords to crossbows and the ability to not be too close to your enemy anymore, we have today in the world of biotechnology basically had an explosion of new tools and new capabilities to do things to microbes or use microbes in ways that we could never have anticipated ten or 20 years ago.

And we can only anticipate that that acceleration of those tools will increase over time. That will, I think, provide access to many additional parties to do things that were unimaginable to organisms ten or 15 years ago, and we're going to have to account for that because today we may put the capabilities of doing bad things, intended or unintended, in the hands of people who may not be professionally or I should say intent-wise prepared to deal with those outcomes.

And so I think that one of the things we're going to be doing today is I liken it to the idea of surfing at Maui. If anybody has ever been at

the high wall of Maui where it's 60 foot waves, if you're too far forward, you're dead. If you're too far back, you're dead. But if you're right on top of the wave, it's a hell of a ride.

And I think our job is going to be riding that wave, to basically figure out how to not slow down progress in taking on the world of microbes, but at the same time not providing opportunities for someone to create great harm from those explosion of tools that we're creating today with our microbes.

DR. LUMPKIN: So if we get it wrong, we're all wet?

DR. OSTERHOLM: No, you drown.

DR. LUMPKIN: I think my role on this committee is sort of as the informed lay person whose job it is to think about some of the aspects, and I think I would like to start off our discussion by sort of charging us with trying to not exclude some alternative approaches because they aren't in existence at this point.

Our overall goal, in one sense, is that balance as Michael talked about. How do you foster

scientific development, which is based upon communications? At the same time, concern about the fact that there are bad people who would like to take that same information.

And in addition to looking at the sort of regulatory way the development of committees, to also look at ways that we may be able to enhance scientific communication in a way that decreases risk, and that we shouldn't exclude that as a potential outcome of the work of this committee.

DR. LEVY: Well, I kind of feel like I might echo what the previous speaker said, but I would really think what would come out of this meeting may be not so much how can we prevent and actually legally affect anyone who wants to do harm, which I think is difficult to think about trying to do internationally, but rather, to improve our understanding of the spread of infectious disease, the spread of microbes, that we do improve diagnostics, that we do improve understanding of what leads to spread so that we actually are setting up good science to protect, not trying to go back to prevent the so-

called bad scientists from doing something which we clearly see is bad.

And I think one of the critical features which was mentioned of hopefully this committee's activity will be to bring awareness to the real needs of protecting people's health.

In my own field, I find the misuse of antibiotics and antivirals to be a real threat. It is a real threat. In fact, we have organisms out there that are killing people and they had nothing to do with biotechnology, just inadequate understanding of what misuse can do and the lack of diagnostics to know what's going on.

So I would hope that what comes out of here is not so much focused on the negative, but focused on the positive, what we can do to improve our understanding of health, disease spread, and in that way really impact what could happen by somebody in some distant area that we have no control over.

DR. FRANZ: Thanks.

You'll learn more about my frame of reference this afternoon when I speak, but it really

began in this area about 18 years ago when I arrived at USAMRID and began working on medical countermeasures at that time for biological warfare agents. We weren't thinking that much about terrorism in those days.

I think it was impacted by the work that we did in Iraq, with the search for the weapons programs under UNSCOM the first time around, and also my involvement in working to reduce the likelihood of the Russians continuing their offensive program under the trilateral agreement and negotiations.

And then in an area I'm still involved, the cooperative threat reduction program that Senators Nunn and Luger and Dominici started in 1992, all of those things impacted the way I think about dual use, and I think you'll see that this afternoon.

I think at this point I have a fairly good sense of the complexity of the biological threat, and it is a very complex problem that we face, and I think from that I've learned that technical solutions alone are not enough to protect our citizens from the abuse of biology.

The other thing I think I understand is that this is a much smaller world now than it was not too many years ago and we've got to think internationally when we're thinking about biological security. I also from my experience believe that building massive sort of regulatory schemes to solve this problem won't be enough, and sometimes those kinds of things actually build walls between people, especially internationally.

And I'm also certain that science is a common language that helps build understanding between people internationally. I need to disclose one strong bias and that's toward balance, and I think we need to balance the technical and the nontechnical. We need to balance the hard and the soft power, and that's sometimes difficult in our system, and we need to especially in the context of this committee balance freedom and security.

Thank you.

DR. ERLICK: Good morning. I believe I'm here essentially to look at both aspects in terms of the problem, one looking at dual use from the

standpoint of those who intend to develop technologies specifically for the purpose to do harm, and deliberately hide them within the guise of what seems to be legitimate research. And I have done that for, as I mentioned, many, many years, trying to put myself and my people in the mind of those who would do so.

And I will tell you it's a very, very complicated issue, and the analysis is quite, quite lengthy and multi-focal.

There's another aspect, too, and it's those who undertake research not knowing necessarily that the research that they're accomplishing might provide aid and comfort to those who are looking for that type of research, and believe me, there are those who are looking at potential research that could be used for illicit purposes.

So I believe that I'm more negative, unfortunately, than some of my colleagues in the sense that I believe that one of the missions and functions of this Board is to provide discrete analysis of what dual use is really about, who might be undertaking that, but balance it in the sense that we do not act

as an impediment to legitimate intercourse, research and other efforts that are ongoing.

I will end up by saying that I believe that a major component of what we're doing is not only U.S. based, but internationally based, and we have to look at our colleagues throughout the world as to what they're doing, and again, the last word I will have is I think, as Dave said, we have to provide a measure of reasonableness as to what we're doing. If we err on the side of providing advice that is too narrow and too severe, then we're going to limit research, and we simply can't do that.

So we have a very tight balancing job to do, and we might fall off the board several times.

Thank you.

DR. CASADEVALL: I'm here as an infectious disease physician. I actually take care of patients, and I do a lot of research, and I'm primarily based in the laboratory, and I'm an investigator.

My views are that biological weapons are here to stay. I don't think that if you look at the history of humanity that humans in conflict give up

things that they could use in war.

However, biological weapons pose a fundamentally different challenge than any of the prior human weapons, and that is because they're ever changing. The host changes and the microbe changes. So you have a situation where with time new microbes come in as well as the host changes.

So in some way, the challenges here are enormous because you're trying to understand and possibly regulate something and possibly that is where the rules are changing. I know we'll ask you to consider how would you go around if you had to regulate nuclear weapons. How would you do that if the laws of physics change on you?

I would point out to you that in a situation where you have great changes happening. This is an area where the defense is very much dependent on research and it is dependent on openness.

And I would argue to you that we show a great human success in 2003 with the containment of the SARS outbreak, and that was something that entered the human population. It was contained within a year,

and it was done so largely because of the openness in which people could communicate with one another.

What would have happened if researchers could not communicate? What would have happened if samples couldn't make it across boundaries? What would have happened if sequences were restricted because this thing was so dangerous?

Do you think that by the end of 2003 the organism would have been essentially contained such that now it exists only in the laboratories and in the wild?

That having been said, I think that we have some real threats and some real bad agents out there, and we need to figure out some way to hit a balance. I am very optimistic. I believe that if you listen to all of the speakers, every single one here up to now, and I'll bet you the other ones after me will do so, will argue for trying to find a balance. Where is the set point?

And I think that with discussion and an honesty and openness we will be able to do it.

ADM. STUDEMAN: It seems to me that the

intelligence community, the defense community, the Homeland Security community, law enforcement, and now the medical and research communities share something in common with regard to this class of threat. While you might have considered all of these organizations strange bedfellows in the 20th Century, in the 21st Century it seems to me that maximizing the interaction between these organizations, breaking down barriers and creating a fairly elegant interagency process is really the order of the day, something that's very difficult for large government bureaucracies that tend to be vertically organized to do. So this is a real challenge.

This threat is unique, obviously. From an intelligence point of view, we deal mostly with threats that come from off shore. The interesting thing about the biothreat is the people who would perpetrate the threat could be insiders or they can come here, and they don't need to bring that threat. They can actually manufacture that threat here domestically.

So from a point of view of the intel

community, as it's now being defined under the new Director of National Intelligence, who has the responsibility to integrate domestic and foreign intelligence, there is a requirement to structure that community so that it's better able to do that job, to transform that community.

And so that community's transformation, as well as its ability to operate inside this interagency process, is important. And that transformation for the intel community is like trying to change a tire on a car while it's moving.

And so clearly I think that the big challenge here is a challenge that is at the strategic level. It's a challenge of policy, but it's also going to be a challenge of interagency collaboration.

CHAIRPERSON KASPER: Dr. Wara.

DR. WARA: I'm here to represent the Recombinant DNA Advisory Committee, a group that was formed in the late 1970s in part because of uncertainty of scientific direction for our country with regard to recombinant DNA.

This group has functioned since the late

1970s and has served to guide both our scientific community and the public in terms of our direction. We've run into bumps along the way. We've almost been disbanded at certain junctures, but because of our focus on education both of the scientific community and of the public, I believe that we've achieved and continue to achieve our goal, which is truly to be certain that balance is reached, a recurrent theme, regarding risk-benefit, the risk being in my mind both to the individual and to our community of the inappropriate use of recombinant DNA technology, and then a second risk which is that in our enthusiasm we might have -- and I believe we have not -- dampened scientific productivity.

We've accomplished this balance of risk-benefit through the individual review of specific studies or protocols; to look at each of these studies for their risk-benefit, and that's what this group really is being asked to do; to look at various aspects of potential dual use; and we've done that through open public communication. Each of our meetings are open, and they're not only open for we,

as RAC members, to sit and discuss, but for those of the public who attend to ask questions, which we actively answer and we exchange in discussion.

We've also done that through a global perspective, especially during the last five years, because both DNA technology, protocols, and bioterrorism, as has been mentioned by others, are global issues. They're not just issues for the United States.

So the guidance that we put forth as members of the RAC, which I hope we'll put forth here, is global guidance, and it's meant to stretch throughout the world in order to, I hope for this group, in order to diminish, probably not eliminate, but in order to diminish the risk of bioterrorism.

DR. RUBIN: There was a very famous professor of pure mathematics at Cambridge, a fellow named Hardy who wrote a book called The Mathematician's Apology, and he worked on a lot of different aspects of mathematics, including theories of random walk, and he was mortified to realize that the British navy used his theories to track

submarines.

And here is a fellow who said, "I would never do anything that would have any practical application."

So in thinking about Dr. Zerhouni's charge to us, he put the context of dual use in a very interesting framework, and that is scientific intent, and I would be the first to admit that I'm going to have a hard time figuring out scientific intent because any of us who work on pathogenesis, and I work on pathogenesis and tuberculosis, almost by definition, if we identify a gene associated with dormancy or invasiveness, that almost by definition means anybody working on pathogenesis works in a dual use environment, and one is going to have to look deeply into, as Woody Allen said, into the soul of the person sitting next to me to figure out what the intent was.

I want to also say that there are rules and regulations and international law that we have to maintain and adhere to both in a legal and a moral sense. So in any of our deliberations, we really have

to consider what the international law is in terms of the kinds of processes and developments that we work in.

The notion of -- and I think Diane really hit on it -- is risk assessment and threat assessment. I think what we have to do in coordination with the community, the public, the intel community, is to really figure out in a realistic way what the threats and the risks are. Put aside all of the hysteria and all of the headline-grabbing and all of the this and the that, but to take a very scientific approach to can we do a net assessment, a risk assessment, a threat analysis of just how dangerous and how will these things be used.

And I think we have to hold ourselves and the community to the absolute highest level of analysis when it comes to that risk assessment and try and put aside some of the fears and the hysteria.

DR. IMPERIALE: I'd like to pick up on the theme of risk assessment because that's what we do as an IBC, is we try to assess whether a particular experiment dealing with recombinant DNA might lead to

release of a recombinant organism into the environment or exposure of a laboratory worker to that organism.

You know, I think as it relates to the topic that this Board is charged with, investigators who are working with, for example, a Select Agent, I think, are clearly aware of the potential dual use aspects of that work and are thinking about that all of the time.

And if we as an IBC are going to have to review that work, then I think that's going to probably be the easy part because there might be some clear-cut guidance that this Board can come up with.

But what I think is going to be a daunting task is how we look at other research that doesn't have the clear implications for dual use, and the reason I say that is that there may be an experiment that sounds absolutely fine and there's not going to be any problem with it, but one of the things that we thrive on as scientists is the unexpected results, and a lot of times one enters into an experiment and you have a hypothesis and you're either going to prove it or you're going to disprove it, but sometimes you come

up with something that you completely did not expect.

And those are the kinds of things that we can't necessarily come up with any kind of rules for or against, and that's where I think one of the important roles of this Board and the IBCs is going to be to increase investigators' awareness just so that people are thinking along those lines so that if a result comes up that may have some implications for misuse, that the person is aware of that and then can deal with it.

And so I think coming up with guidance as to education of investigators is going to be another important role of this committee.

And then the second comment I would just like to make is to reiterate what many of my colleagues have said, which is because it's so important, and that is that the progress of science for the benefit of mankind is so absolutely dependent on open communication of results that I would make the argument that in the vast majority of cases, the good that would be gained from communicating results will far, far outweigh the potential for misuse.

And I think we really do need to keep that in mind as we deliberate.

DR. RELMAN: I would simply start by acknowledging that I believe there to be credible threats that stem from the wanton or mischievous use of science, and I think it's important for us to publicly acknowledge that, but it might also be important to recognize that perhaps the most likely threats will come from not those who set out to intend or deliberately cause harm, but from those who are simply mischievous or careless and might not have had that acknowledged intent to start.

And I think it's also important for us to recognize that the problems that we must grapple with are clearly resonant with the general public. They see this as an immensely important issue that must be dealt with in a serious manner, and I think it behooves us to acknowledge that concern and deal with it appropriately.

So having said that, I would make three very simple further statements, and some of which are somewhat repetitive of what's been said.

The first is that the current scientific enterprise, although immensely powerful and productive is potentially fragile, and it's also precious, and it is easy to damage. So I would first suggest that we follow parts of the Hippocratic Oath which suggests that at first we do no harm to that precious enterprise.

Secondly, I think it's all too easy to become trapped in the examples and mindsets of the past. We often harp on events or activities that have preceded us as guidance for what might be important or what we should do.

Science is moving incredibly quickly. It's evolving in a way that we can only begin to imagine, and we certainly can't quantify easily, and I think it's important, therefore, that we strive to maintain a future base perspective on what constitutes a potential risk, what is actually an important parcel of the good that comes from science.

Finally, I would repeat what I think David Franz introduced, and that is the notion that we work in a seamless global community and much as we would

like to think we have some control over the scientific enterprise here in this room or in this country, we really do not. And I think what we can best hope to do is simply influence the way in which our colleagues and the community and the public think about these problems, sensitize them, and cause them to deliberate over some of these issues that may not have come to their attention.

So I'm optimistic that this Board can be helpful and can do some good.

Thank you.

MR. NANCE: Knowing that I'm an attorney, you might be surprised that I harbor a certain degree of skepticism about the ability of additional laws or regulations to deal with the problems that we're addressing here today. I think this truly is a challenge without borders and one that challenges the ability of traditional notions of law and law enforcement to deal with the problem effectively. It is a profound risk, and I believe that we must put our intellectual capital to its highest and best use and in the interest of doing no harm to insure that we

develop new and improved methods of prophylaxis, detection identification, and treatment to confront what I believe is an increasing risk and one that could result in disastrous consequences.

I believe the work of this committee must be focused on insuring that the forces of good can function in the freest and most effective manner with an eye towards insuring that our adversaries are limited in their ability to exploit audits of our ever expanding circle of know-how and technology.

DR. MAHMOUD: It's clear that this Board is facing a very humongous task, and there's only one idea to reflect, which is the combined brain power and wisdom of the group and the community at large is the only answer. I mean there's no discovery here. There's no invention.

I just want to reflect on three dimensions to the issue, and all three have been mentioned in one way or another.

One is that as John Donne has said many, many years ago, no man is an island, and we are not alone. This is an international issue and is not

going to be solved by one country or one community. The security here is global, and the issue is global in many, many ways.

We all are concerned because the second dimension is innovation. What brought humanity to the year 2005 with all of the tools that we have is the phenomenon of innovation, which is by necessity as widespread, is over dispersed in the human community, in the total group, and it is very, very dear, and it's a very important phenomenon, and it has to be protected, that innovation is not the property of a single body. It's a property of the total human effort everywhere in the world.

The third element, because of where I am at this point, industry and particularly the pharmaceutical industry, is a major, major important element of what is happening in this world, and consequently, it would be important to see that the point of view and the implications on a significant segment of our, again, the total human effort to find, discover, and bring on solutions to some of the major health problems is part of our thinking.

Thank you.

DR. LEMON: It is very difficult to be the 16th or 17th individual to be asked to comment on this because I agree with everything I've heard so far, which heartens me greatly.

I do think that the threat is real. I do think that the answer to the threat is going to come from additional research, and that it's very important, absolutely critical as we go forward and deliberate these issues that we preserve the ability for our research community to address that threat.

We were asked by Dr. Zerhouni to consider the needs of the research community while preserving national security, and I just want to emphasize that the research community serves the national security and I think very well.

I think preserving the scientific edge will be essential to stay ahead of not only manmade threats, but threats by the worst of all terrorists, Mother Nature, who keeps throwing them against us, whether it's SARS or avian influenza.

I also think that as a committee, we have

a real challenge to help the broader public gain an awareness of both natural and manmade threats and the role of science to address those threats. I think science is under siege from a number of quarters, and it's very important that the public understand what science can and cannot do, and I think this committee can play a role in doing that.

I just want to close by reiterating the fact that we live in a global community and nothing that we do here that has a simple national focus is going to succeed, and we really need to keep that broad global viewpoint.

Thank you.

GEN. GORDON: We're going to be even one more in the line of speakers, and you could also be sort of the only physicist and the only nuke in the group of physicians and biologists and veterinarians, but I would offer a comment along the lines of the importance of the committee and all we have to do. And in sort of paraphrasing what Dr. Zerhouni and the Chairman said, to provide advice and oversight in a way that offers real security and supports a strong

and very aggressive research agenda.

And if I could use a double negative, I would note that it's not a natural state for our most senior policy makers to not act and to not act aggressively when faced with a very real or a perceived threat. These policy makers take very seriously what must seem to most of them as their most solemn responsibility, and that is the protection of Americans, and so they're naturally inclined to react very conservatively, very protectively, very restrictively.

And so if we're not successful in this group and other groups in finding the ways the Chairman and Dr. Zerhouni suggested of both finding the right set of guidelines and, maybe even more importantly, inculcating a different culture, a real culture in this, we will find the restrictions on the research which I think we want to avoid.

I don't want to disagree with what anyone else has said along the lines of balance, but I wonder if we would just sort of try to keep our minds open of what the concept of balance means. Sometimes to me at

least balance suggests that we are giving up one for the other, and we have to give up freedoms to be able to have stronger security or the other way around.

I wonder if we can at least keep our minds open up to the possibility that we don't have to think about a balance, but there may be some opportunities that both strengthen security and encourage a very aggressive agenda.

Thank you.

DR. ENQUIST: I believe one of the reasons I was put on this committee and I accepted is because for the past four years the American Society of Microbiology and, in particular, me as the Editor-in-Chief of the Journal of Virology, the top virology journal in the world, have been dealing directly with the issue of should we or should we not publish papers, and I wanted to take my two or three minutes here to tell you what we have done to give you a little set of facts anyway of the kind of problem that we're facing.

The American Society for Microbiology publishes 11 journals, all in the area of microbiology

and the Journal of Virology is one of them. We're a professional society often seen as the source of advice on microbiology to our government and also to other international agencies.

In the summer of 2002, I became the Editor-in-Chief of the Journal of Virology and was also then made aware very quickly of the public concerns about anthrax, synthesis of polio virus, making more virulent viruses, and during that summer, the ASM decided that we wanted to let the American public know that we take the problem of biosecurity very seriously even though we had zero guidance on how to proceed.

So we began the process of instilling a culture of responsibility at all levels at ASM in terms of at least doing research and publishing research.

We had several calls that summer, conference calls. I was at Woods Hole trying to write a textbook on virology and I was also working on these conference calls with the 11 editors-in-chief of the various ASM journals, ASM public affairs, the senior

leadership of the ASM, and basically we came up with a two-part system for dealing with publication scrutiny.

And the other thing that we did was that we wrote a position paper asking the National Academy of Sciences to give us some guidance as to what to do. And as a result of that, there was a meeting of all of the editors or at least participating editors that published scientific work in Washington, D.C., sponsored by the National Academies to discuss this problem, and there was also then the National Academy put together the so-called Fink report, which gave us some guidance of things to do, but that took several years before that showed up.

Basically the system we use is really very simple. There are two parts to it. The first thing is that every paper that goes to the Journal of Virology is reviewed by members of 200 members of our editorial board or about 200 ad hoc reviewers. There's a little check-off box on the review sheet that says, "Do you think that this paper in any way has science that could lead to misuse?" If that box is checked, the paper comes to me, and to the

Publication Board Chairman, and then we discuss what we're going to do with that.

The second thing is that the Select Agent list is well known and the publication staff of all of the ASM journals flag every one of these Select Agent's papers, and depending on which journal that they're in, every one of those gets looked at by the editor-in-chief, and if there is something that there's a question about, we discuss it with the Publication Board Chairman.

Just to give you a little bit of data here, in the four years that I've been involved in doing this, the Journal of Virology has looked at over 15,000 manuscripts. About half of them have been published, accepted. The other half have been rejected for scientific purposes and I suspect that almost all of those that were rejected are published in some other journal somewhere or published on the Web or whatever.

You need to understand that the bottle has many holes, and we're only one cork in the system.

The Select Agent manuscripts that we have

published that we've looked at, there were 651 Select Agent manuscripts. We reviewed and accepted 364 and 168 of those were from non-U.S. authors. Two hundred and 87 were rejected on scientific grounds.

The ASM journals in total, all 11, there were about 1,000 papers on Select Agents that were accepted and 768 were reviewed and rejected on scientific grounds.

Of the Journal of Virology papers that we looked at, we didn't identify any one that had a potential for misuse. There was one or two that came up from one of the reviewers or asked questions about virulence studies. As was mentioned before, when you study pathogenesis, you invariably are focusing on the genes that increase pathogenesis because when you knock them out, you lose pathogenesis, and so we had to deal with those.

I think for all of the ASM journals there were two or three papers that were flagged, and that were subsequently debated, and either the papers were rewritten or were subsequently approved.

The bottom line here is that this concept

of dual use, at least at my level, is a real misnomer because it's not a binary process. It's not black or white. There's nuances of understanding of what the science is going to be used for, and that we have a very difficult time in deciding where the balance is going to be.

The problem is that there's a disconnect between the information that's in the paper and the use of that information. We're pretty good now at deciding whether the information is scientifically accurate, can be reproduced, and is good science, but we can't tell what is going to be in the hearts and minds of the individual that may want to use that science, and that's one of the things that we're looking for in terms of guidance here.

So I thought I would just end here by saying that this Board really has a job in front of it in order to look at the real practical problems of the fact that we publish thousands and thousands of papers every year that deal with this, and not only in the biological sciences, but also in areas of mechanics and physics and whatever that could have potential for

problems, and so we have to get, I think, a spirit of responsibility at the level of the individual scientist and then in the individual organizations so that we don't stifle the scientific enterprise, which has been noted before and is really my mantra.

It's a very fragile enterprise. It's the reason why we're so powerful, and we can't let this enterprise go south because of conservative views.

But, on the other hand, we really understand that there is a serious problem that's facing all of us in terms of the misuse of science. And so we have to get the general public to understand that we're trying. We have to have some rules and some guidance that lives up to this idea, and I'm looking forward to participating in this process.

DR. COHEN: I have a somewhat different perspective to offer coming from my 30-year public health career focused on prevention of occupational transmission of infectious diseases.

For me it was a very sobering perspective that four of the five deaths from the anthrax in the mail bioterrorism in 2001 were due to exposures at

work. Much more likely scenarios than bioterrorism as we know it are scenarios related to safe operations of the high containment laboratories where we are doing the research. These would include accidents, operational or mechanical or maintenance failures, sabotage or theft of research.

Concern about how we work in biological laboratories is just as important to national security as concerns about what work we are doing in those laboratories. The perspective I'd like to offer to my colleagues on this Board is that we not overlook the obvious in our high minded analyses. We can accomplish a lot of new national security by renewing attention, vigilance and even expanding the existing by developing additional principles and practices of safe science in doing good science.

DR. SORENSEN: I'd like to offer a parable from which I derived several morals, and in the interest of brevity, I'll just present two.

I recently led a delegation of university administrators and faculty to the People's Republic of China, and it was an exploration of reciprocal

research agreements, exchanges of scientists from Chinese universities to American universities and vice versa, graduate and undergraduate students as well.

I was struck by the fact that I've been visiting various countries in Asia for several decades. The openness of the Chinese scientists to the prospect of collaboration was unprecedented in my experience. Prior to going on the trip I had read an issue of Nature that was devoted to avian influenza, a very sobering analysis of the devastating effects that might be the result of that epidemic if it's not checked, and among the contributors was Mike Osterholm, who is one of our panelists, a member of this Board.

So two morals that I derived from that. One is to establish the balance between the openness and the classic traditions of the academy of the need to protect national security, which I thought Dr. Franz stated very succinctly and was echoed by many other members of this Board.

Another moral that I didn't hear referred to is that balance is a necessary, but not sufficient

condition. Communication of the balance must be conveyed with adequate nuance and yet very clearly.

Now, I know 100 percent of the journalists who are present here are highly sophisticated, sensitive and can, indeed, do that, but the prospect of talk radio, talk TV, blog sites, tabloid journalism focusing on the antipodes that we're dealing with, the one extreme of we must not inhibit any communication or any scientific discussion, and the other that we must be highly restrictive and highly protective.

The likelihood that they will be distorted is enormous, and given the fact that Dr. Kasper outlined five task forces or committees that will be formed, two of them could potentially deal with this issue directly, communications and international, and we might benefit in those committee meetings from having people who are experts in communications talk with us about not only what conclusions we arrive at based on our considered judgment, but how we communicate that to the world at large.

CHAIRPERSON KASPER: We're going to interrupt these introductory remarks before we move

to the ex officio members. I will go on to ask them to speak, but we're fortunate enough to have Dr. Rajeev Venkayya with us today. Dr. Venkayya is a Special Assistant to the President and Senior Director for Biologic and Chemical Defense at the White House Homeland Security Council.

He was a Director for Biodefense and Health at the White House Homeland Security Council from October 2003 to May 2005, and played a significant role in the development of U.S. government policies and biosecurity, biosurveillance, public health, and medical preparedness, and the national biodefense strategy.

So we're very happy to have you here with us today to give us some of your thoughts on this area.

DR. VENKAYYA: Well, thank you, Dr. Kasper, and thank you all for indulging me in interrupting the presentation. Fortunately, I didn't interrupt the real members, just the ex officios whom I work with every day. So they can bring it up at the next meeting, I suppose.

I do appreciate the opportunity to give you a little bit of background to what led to this meeting today. There is a parable there that I think is worth keeping in mind, which I'll get to at the end, that resides within the story of how the NSABB was established. I want to first though make it very clear that from the very start of the discussions around biosecurity in the summer of 2003 there was significant interest in the issue at all levels of government, particularly at the White House.

And I can tell you that in the summer of 2003, in light of the news that was coming out of the Department of Energy and Dr. Venter's lab in follow-up to Dr. Bremmer's work and follow-up to the mouse pox work, there was an increasing sense of angst around government, around what our policies were going to be with regard to dual use technologies that were rapidly advancing and would eventually bring us to a point where the technology to do big things, good and bad, would reside on the benchtop of scientists around the world.

Right around that time the Homeland

Security Council, which is an analogue, a domestic analogue of the National Security Council, convened a group of federal partners to talk about this issue, and it just so happened coincidentally in what is a remarkable alignment of the stars that the National Research Council was about to publish its report on dual use technologies and life science research.

Now, I have never seen this happen before. I've never seen a professional community be so far ahead of the curve that two years ahead of this discussion at the White House they had already begun the process of drafting what the professional community's opinion and perspective and recommendations would be around this issue.

It took two years to get to their set of recommendations, but I can tell you that were it not for those recommendations arriving at the time that they did, and this led to briefings at the Department of Health and Human Services, as well as briefings at the White House with cabinet secretaries, by the NRC, by Drs. Alberts, Fink, and Atlas, who knows what the government would have come up with.

We have a lot of smart people in government in any administration, but left to their own devices, they are going to come up with a solution one way or another, and we all benefit when that solution is informed to the maximal extent possible by the technical considerations that came out of that NRC report.

And as you map the NRC report against what the government eventually did with its biosecurity policy that was announced by Secretary Thompson in spring of 2004, you'll find that there are great parallels between the two documents.

Secretary Thompson, I can tell you, put forth a policy that was drafted through an interagency process that proceeded very rapidly, led in coordination with the Office of Science and Technology Policy and the Homeland Security Council under the leadership of General Gordon, whom you see before you.

Those recommendations were adopted by the interagency. An MOU was signed, and we have the announcement. The most visible representation manifestation of the biosecurity policy, which is

bigger than the NSABB, I should point out, is the NSABB. This is what everybody thinks about when they talk about the U.S. government policy and biosecurity.

And while I think many people breathed a sigh of relief that the U.S. government did not come out with an over reaching, draconian approach to biosecurity. No one should go to sleep thinking that the U.S. government has stopped thinking about this. The U.S. government has anxiously awaited the convening of this body to answer questions that come up every day around biosecurity.

I can tell you I did not get milk in my coffee today because of considerations that have been raised in the past couple of weeks.

That's a joke. I did get milk.

(Laughter.)

DR. VENKAYYA: Clearly, we are going to continue facing these issues. These aren't going away. As technology advances, we will increasingly have to have these discussions. These need to be informed by individuals that are thinking ahead of the curve.

Let me just leave you with three issues that I think you should keep in mind as you're going forward. First of all, the body that you see above you is comprised of individuals from around the community. It's also comprised of ex officio members from around the government. I want to make it very clear that we view this as being an interagency process that reaches well outside and beyond the bounds of the U.S. government, but also all the way across the U.S. government.

This is not just an NIH thing. It's not just an HHS thing. NIH is kindly the executive agent, and the Secretary of Health and Human Services has ultimate authority over this body, but at the end of the day, this group is going to be advising the conduct, funding, support of life sciences research across the U.S. government.

Every cabinet Secretary is going to be listening to what you say, and they're going to be taking your recommendations seriously as they make their decisions on what to do about experiments that raise biosecurity concerns.

Please keep that in mind. Please keep in mind that you're not just dealing with the research that is supported by HHS here.

The second thing I will say is that the parable I mentioned in the beginning of this discussion about how we should all be thankful that the NRC came forth with its report at the same time the government was thinking about these things continues to apply, and to the extent that you can be forward thinking in your approach about these issues rather than establishing approaches that don't move the ball forward, don't bring the security and science communities more together, you should be doing that. You should have answers ready before the questions arise because you will be aware of the concerns well before they make it to the front page of the Washington Post or The New York Times. There's no question about that.

This group is well aware of the issues that we're going to see a year from now, and you should be talking about those now. I'm glad to see that the synthetic genome issue is on the agenda. I

think that that is one coming down the pike. There are many others.

And the last thing I'll leave you with is that ultimately no matter what we do, what we the U.S. government does, what any government does, what any professional organization does, what any company does is irrelevant if the individual scientist does not have at his or her core a sense of what the right thing to do is.

Now, I know that there is some debate as to whether or not we need codes of conduct. I don't know how much traction that debate has as far as whether or not there should be a code of conduct. I can tell you that coming out of the medical community that it rolls off one's tongue that a physician will do no harm.

Now, I've gone through a couple of very good scientific institutions, and I can't recall explicit training in biosecurity considerations, explicit training in ethical consideration. That's not to say that we do not behave in an ethical manner. It's not to say that every single person I worked

with did not behave and conduct their efforts in a scientifically and ethically responsible manner. It's just that it wasn't part of the curriculum.

And so before we dismiss the idea of whether or not we should have a code of conduct, I think we first need to have a code, and whether that is informed by these efforts or whether it's done in collaboration with others makes no difference. We need to have something, a set of principles that we can all sign up to, and then we need to infuse the educational systems around not only the government, but around the world so that every person coming out of training understands that this is a core tenet of the work that they're doing, and this should be implicitly part of every bit of work that's done at the benchside.

A PI should be aware that these are important things. A PI should be communicating this to his disciples whether it's a postdoc, a graduate student or a laboratory technician. So I view the single point of failure, frankly, as being the individual scientist. I don't mean that in a bad way.

I actually mean that in a good way.

I think that to the extent that we can do all of these other things that we're talking about, but at the same time insure that we build this common set of principles and promulgate it, we will all benefit from that.

So with that, I've taken enough of your time. Thanks very much for the opportunity to speak with you. Enjoy the meeting.

CHAIRPERSON KASPER: Thank you very much.

I think we'll continue now with the ex officio members. Dr. Rexroad, why don't you start?

Thank you.

DR. REXROAD: Thank you.

Each of us today has been directly or indirectly touched by a product of agricultural biotechnology. They are pervasive. They will become more so during this century of biotechnology, during this century of the genome.

As we sequence genomes for agricultural commodities, and we're doing that on a daily basis, we're also doing it for pathogens. We're doing it for

bacteria that are beneficial.

As we do these, there will be more and more opportunities to use and to perhaps misuse these products of biotechnology. So the challenge is great, but one thing that I would like to say to this committee is that the challenge has been met before. If we look at the RAC committee, if we look at the way that biotechnology based foods enter into the marketplaces, if we look at the regulations imposed by FDA, EPA, and the Department of Agriculture for the oversight of the use of the products of biotechnology, we see great successes.

So I think that we can also expect that the results of this committee will help this government and provide us great successes in doing two things.

One is meeting our institutional responsibility to take advantage of the genomics information, to promote science and also at the same time not to provide weapons.

One of the things that's my greatest concern, and it's the same thing that Rajeev talked

about, is the individual investigator. This is the critical point in all of this. We know that if we raise children that behavior modification is probably the greatest challenge in the world. So we're really looking to you for policy, for ways to behave to change behavior.

As a lab bench scientist at one time, I know there are two things that sometimes seem to get in each other's way. One is accountability and the other is creativity, and I think of all the things that we want to do is that we don't want to slow down the creativity of American scientists as we take on this challenge.

So I think it's a great challenge that this committee has. I think there are many things that we will be able to use. I've already had many inquiries from different groups about how we're managing this dual use system within the USDA, and I will tell you that we are waiting to hear from this committee your recommendations both on policy and activities that we need to take on.

So thank you.

DR. HENKART: As I mentioned, the National Science Foundation has as its big picture mission seeing to the long-term welfare of scientific research and education in the United States, and so one of the things that I think we need to do is constantly be scanning the horizon for gaps in the science that underlie our ability to deal with the natural or unnatural threats that are posed both to humans and agriculture and the environment.

One of the areas that we think is very important that hasn't had much attention so far is the ecology behind what microbes are doing in nature as well as in human beings. I appreciate Dr. Relman's mention of microbial ecology within the human, but the ecology of microbes has a great deal to do with what emerged in terms of new diseases of both plants, animals, and humans. That's an area that I think we need to be sure is encouraged and not inhibited by anything that goes on here.

The other element of our mission has to do with education and looking for the future of science. A lot of scientists come from undergraduate

institutions and from undergraduate education that incorporates the ability to do research.

One of the kind of scary things that occasionally crops up when we seek proposals from undergraduate institutions about projects that undergraduates are now doing are the range of very sophisticated kinds of research that can be done with relatively small amounts of funding and with very little infrastructure.

We want to be sure that we don't do anything to discourage the ability of undergraduate institutions to promote the integration of research into their educational activities. Small, non-research run universities have a huge role in training the next generation of the public, which should be scientifically literate as well as the scientists of the future.

And when we're considering the issues of balance, we want to be sure to take into account the possibilities for misunderstanding or for chilling the effect of science on education, as well as just on research itself.

DR. LOMAX: I'd like to point out some of the areas of synergy with things that we do at NASA with this committee, both areas where we can provide some expertise, but I think more importantly, where we can gain from what this committee is going to be doing, what the Board will be doing.

The most obvious one for us is the area of planetary protection, and that's where we're thinking about both mitigating the forward contamination of other planets as we go to explore there, but also thinking about the backward contamination of the earth as we have return missions that we're expecting to have up ahead.

And so we spend a lot of time working on both what kinds of environments organisms might be able to survive in, but also how to detect them and how to make sure that they don't contaminate areas that we don't want contaminated.

Along with that is also we have our crew members working in closed environments with very little chance of egress, and so we need to be very sure that we don't bring organisms that are

questionable into that environment, and so we have a large effort in environmentally monitoring and control and some of the technologies that have spun off of that are currently state of the art for anthrax detection even though that wasn't what we intended them for. The technologies are very similar.

And another area is astrobiology where it's the study of the search for life in the universe and, again, thinking of life's signatures and how we detect those, but also as part of that our researchers are going out and looking for life in the most extreme environments on earth, and as for things like deep sea vents or antarctic ice floes and places like that, and then there's always the potential there to discover unique kinds of organisms which could have biosecurity potentials and problems and how we handle those.

Another area is on disease alteration in space environments. There's unique aspects of space environments like microgravity and kinds of radiation that we don't have here on earth, and what we have found is that there are alterations, especially in microbes in those environments. We see increases in

virulence and decreases in the human immune response which could have potentially disastrous results. And so it's an area of active work for us.

And then finally I mentioned the environmental monitoring and control, especially on places like the International space station, but one thing that we can perhaps bring to this committee is several have mentioned that this is definitely a global issue, not a federal issue, something where we need to work with our international partners on this and someplace where we have and can bring perhaps our experience from the international space station and the 16 international partners that we work with there on issues that are similar to this.

DR. WALTERS: The availability of the tools and the skill sets for use in biowarfare and bioterrorism is huge, and the intentions of our adversaries are malignant. The intelligence community that I serve has a global responsibility, as you know and as you've heard, and the acquisition of useful information is truly daunting for us.

Activities in which we would have and will

continue to have an interest are easy to hide and there are a lot of places to hide them.

That said, I'm going to take an optimistic case that this group, this Advisory Board, will define the appropriate policy and ethics environment. However, if we are to maintain openness and placing information in the public domain, then the science and technology in which we engage and which this country sponsors must absolutely be preeminent.

If we fall behind, we will have a very, very steep price to pay. We don't expect this struggle to be either easy or short. We look to the eminent individuals that are serving on this advisory committee for a balanced opinion put forward in an environment in which it will be acceptable to the participating agencies as well as citizens of our country.

DR. KERR: I'd just like to echo the historical perspective of my colleague from HSC, Rajeev, when he was talking about in the summer of 2003 when all of this really began within the White House and General Gordon, as Assistant to the

President for Homeland Security, and Jack Marburger, the President's Science Advisor, really tasked the Executive Offices of the President to really offer options to the President for consideration of how do we deal with this encroaching security risk posed by dual use life science research.

And so when we gathered the federal partners and began to examine the deliberations and, again, our thanks to the National Academy for their years of work that had gone on in the private sector and in the scientific community to offer their deliberations, it really is good to understand that there were a wide variety of options that were offered to the leadership, everything from do absolutely nothing to the opposite end of the spectrum where there were options that were extremely harsh, draconian, legal, regulatory measures that really would have brought about security and brought science to a crashing halt, and we recognize that.

And so the President chose a balanced option that actually created this body, and so it was with that deliberate measure that bringing together

the variety of subject matter experts and disciplines that are represented on this body, we are very, very eagerly waiting the deliberations, the advice, the recommendations, the best practices that we have not only to offer to our federal government agencies, but also in the way of best practices that can be extended to the private sector, as well as to international governments and businesses at the international arena so that we can address this global risk posed by the misuse of dual use, life science and biotechnology.

DR. JUTRO: I work for the federal government. So as do all of my colleagues, we spend a lot of time in meetings and on advisory boards, and frequently there comes a point about halfway through a session like this where you start thinking to yourself, gee, everything has been said. It's just that not everyone has said it yet.

That is so not the case here that I've been awed. Literally everyone has made a genuinely unique intellectual contribution to the discussion. I'm going to see if I can keep that up mildly.

My thought is that in the history of

science and national security's relationship, most of the lessons that we have in the literature come from our work with nuclear materials and in biology with Select Agents, and one of the things that controls that discussion is a limited amount of comfort that we historically had with the fact that these are either difficult things to make or difficult things to get.

The problem with the life sciences is that we've kind of created a twisted metaphor of the philosopher stone. We have now made these things extraordinarily accessible. The tools are extraordinarily accessible, and it is reasonable to believe, as my colleague from the National Science Foundation said, that not only are these things already the tools to do life science research, already in colleges, but I wouldn't be surprised if it's not too many years before we see this sophisticated ability in high school laboratories.

Given that, the question then becomes is it only the intentional adversary that we have to think about, and as my friend David Relman said a moment ago, no, it's probably not. We have to worry

about the mischievous. We have to worry about those who are simply curious and perhaps especially among those, those who perhaps are not old enough to have quite yet developed a fully functional superego.

Given that, we have a couple of lessons. Are we in the same place as computer sciences was about 20 years ago with hackers? I mean, computers have shown us that doing something that is bad does not require malice in the same way that nature shows us that doing something bad in biology doesn't require malice.

Given that, I'm not sure where we stand with regard to the need of a code of conduct, but we clearly have to look at what the importance is of influencing educational policy and public opinion on the issue and explore questions that have to do with how we teach a sense of responsibility, hopefully quite early on in the educational process, and export whatever curriculum or whatever ideas we have developed in this country as broadly as possible.

DR. CUCCHERINI: I'm mostly impressed with some of the thoughts that have been expressed this

morning. I think mine may be just a little bit different.

VHA's research program is an intramural program, and its primary goal is to benefit and enhance the health of the veterans and then secondarily of the nation itself. Our program of research encompasses everything from very basic research, from immunology, infectious disease, and on and on and on to clinical trials, translational research, and health systems research.

We have over 120 facilities that conduct some type of research, and many of them are affiliated with an academic institution. Our investigators are as varied as our research is, and some of them work full time for the VA. Some have academic appointments and work part time for both the VA and then the university.

We have a number of challenges, one of which is that recognizing that our research is to benefit the veterans and his and her health, the challenge is to also recognize that our good intentions may end up with research that we could

classify as dual use research, and we, therefore, then have to give our investigators and even our administrators tools to recognize what dual research is and how to minimize it while still continuing with the research that we need to do to meet our objectives.

The other challenge in this area is that we need to be able to change the area in which we're doing research based on the needs and maybe I should say misdeeds of others; that we should be able to, and I think we can respond rapidly to new threats to our veteran's health and our nation's health.

The other real challenge for us is in security of our facilities, of our data, of our resources and trying to balance that so that we don't decrease our investigator's ability to collaborate with others outside of the VA, to have access to all the resources that they need, and to sort of control the access to our facilities.

The biggest challenge of all, and I think this is where this advisory panel will be the most help to us is trying to identify where we need to set

our policies and our standards related to these issues, and again, with the thought that we don't want to make it harder for people to conduct the research that is so important to our nation, but yet that we really want to make sure that there's no misuse or that dual use of research.

Once we sort of get an idea of where we want to go with our policy and our guidance, then the other important issue is going to be developing the educational programs to go along with that, again, that will address some of the ethical standards and will address ways to identify dual use, that will teach them how to sort of change gears fast and refocus research in areas that would be needed because of some very negative things that can happen in our environment and from other people.

DR. STEELE: First, I'd just like to say that the Department of Justice and particularly the FBI is very pleased to be a partner in this endeavor. Obviously we believe we are already in the midst of some very challenging and very important issues in the areas of biosecurity, biodefense and dual use

research, and we are looking forward to this body and helping to clearly define those terms as we move forward so that when we discuss biosecurity we're all starting from the same baseline as we move forward.

In addition, as an Advisory Board, as opposed to a regulatory board, we see a critical role for this body in increasing the sensitivity and awareness of these issues really across the scientific, law enforcement, and intelligence communities, and I think having such a broad representation of diverse disciplines on this group will be a tremendous asset as we move forward, and again, we're very much looking forward to being part of that process.

And discussing partnerships, I think this Board also provides a very good opportunity to increase the partnership between the scientific community and the security community, national security and Homeland Security communities.

And I parallel that to some of the work that we've been doing between law enforcement and public health, particularly between FBI and CDC, but

also at public health and law enforcement across the state at the local and federal levels.

Obviously we rely on the public health community to identify a suspicious outbreak or a case that may raise that index of suspicions and trigger a notification where we can jointly investigate that case to determine if it has some criminal nature to it.

In the same way, the scientific community would really be the first to recognize suspicious activities within the research community and obviously rely on them to monitor that activity and provide a mechanism to raise that up.

And I think that also ties into the culture responsibility that Dr. Zerhouni and Rajeev mentioned earlier today already and the critical importance for that.

But despite the challenges that we have all discussed already, I think this body will be in a unique position to address a broad range of issues related to biosecurity as we move forward and provide some much needed guidance, and back to the surfing

parallel, hopefully we won't drown in the process.

CHAIRPERSON KASPER: Dr. Vilker.

DR. VILKER: You caught me daydreaming there. I thought you were going down there.

(Laughter.)

DR. VILKER: But daydreaming on the points being made. Excellent discussion.

CHAIRPERSON KASPER: I'll try not to take that personally.

DR. VILKER: No. I realized as I was saying it what was coming out.

I guess I won't wax and wane philosophically here. I think there's been a lot of germane discussion along those lines.

As the representative from the Department of Commerce, I explained earlier that my role is to represent particularly the scientific elements of DOC, which is NOAA and NIST. I come from NIST. So I'll say a little more about that, but I would like to offer that the marine environment -- I won't say it's not represented here. That would be very foolish, but I think the intensity of its representation is not as

manifest as it could be by bringing in a representative from NOAA, and perhaps off line we can deal with the marine environment a bit later.

I'm reminded of what red tide is doing to the New England fisheries right now, and although most of us have alternative places to get clams and oysters, there's a big segment of the economy which is paying a dear price for something which nature has inflicted on us but wouldn't be that difficult, I suppose, for someone to dream up a more deliberate manmade scheme.

NIST is very familiar with dual use technologies. First of all, we derive most of our work statements from other agency missions or the facilitation of science, scientific discovery and technology into the marketplace. Sometimes we work more directly with commerce, with industrial partnerships.

But other agencies still represent the majority of the kinds of work that goes on at NIST, and I'd like to give two examples, one which is unrelated to biosecurity but perhaps the train of

thought will be stimulating in some way, and the other one which, I believe, is more directly related.

The first one, more than three decades ago people were asking the question of how well we know time, and, well, gee whiz, we had that down to ten or 12 decimal places. What more do we need to do?

Well, it turns out that those people who were thinking about satellite communications really needed to bump that out about three or four orders of magnitude.

So NIST invested and the Department of Commerce invested a fair amount of capital into striving for that. One cannot -- I mean, we take for granted now satellite communications, DIRECT-TV, et cetera, et cetera, and yet that is critically dependent on how well we can synchronize signals, and we do need to have those 13 or 14 decimal places in time.

Well, the effort to do that led to the discovery of a new state of matter, the Boze-Einstein condensate, and that has further stimulated thinking about the last artifact that is left in the

measurement world, which is the kilogram. There still is a piece of material sitting in France which gets taken out about every 30 or 40 years that weighs one kilogram, but that's not good enough anymore, and so there's a great effort to use our discoveries and our research in atomic physics to find a non-artifact measure of weight.

About five years ago we were asked -- this story number two, which I'll end with, is we were asked by a part of the Department of Agriculture to help with the measurement of genetically modified grains in a mixture of grain. We were challenged by the European community to find basically one kernel of corn in a boat load of corn which had come from a genetically modified corn plant.

Now, more than half of the corn grown in this country is genetically modified because it's such a great advance in the way we can control diseases in corn and how we can produce the huge amount of corn that we do.

Well, we started a project with the Department of Agriculture to benchmark real time PCR

methodology for finding that one kernel in that boat load of corn, and there now has been advanced quite a bit of reference materials and technologies which are helping the world make those kinds of measurements.

At some point this is probably one of the leading technologies that will be used to discover microbial insult in a rich microbial environment.

So those are the kinds of things that NIST gets involved in. We need other agency partners to define a problem and to help us explain the measurement issues upon which the discovery, the detection, the quantitation become a critical element of policy, of public health, or of health in general.

So thank you for the time, Mr. Chairman.

DR. NIGHTINGALE: Okay. Thank you.

I have a few brief comments to make on behalf of HHS.

It's clear that this is an extremely important Board. The advice is very important to us and to the whole federal government and to the world. There's no question about it.

We need to have new countermeasures for

CBRN threats. We have to have new drugs, vaccines, diagnostics for public health threats of various types. We certainly are concerned about balance and want to promote the scientific enterprise to make sure we have these. At the same time we want to make sure that the national security is protected.

I'd like to say a few words perhaps about the urgency of this. We've all, of course, been waiting for this group to get together and to offer advice. We need to get the advice. I think a tremendous pressure will be placed on the working groups to come out and actually provide the advice. There will be a challenge, of course, in terms of the integration and the response to the advice by the various heads of the federal agencies, and then there's the challenge that Ambassador Turner mentioned in terms of how to get the advice and recommendations, good practices, et cetera, implemented, how to get them to the right international bodies, for example, how to do the right thing domestically.

And I think a challenge for the Board, in particular, is the fact that this is not a de novo

situation. There's a great deal happening as, of course, has been expressed by many of the experts here who are doing things related to, for example, the communications issue.

We know that many of the international organizations are already actively engaged in codes of conduct, OECD; WHO is involved; the biological weapons convention activities relate to this. So there will be a real issue about drawing on what is happening internationally and domestically integrating this into the work of the working groups and then bringing that back here to the Board as a whole.

And we're fortunate to have the experts on this group that we do and people who are directly involved in these both domestically and internationally.

So I think there are these major challenges. The urgency of getting this done and then the process issues in terms of working the various groups, coming up with recommendations and then getting these disseminated and adopted.

Thank you.

DR. KLEIN: Thank you.

One of the challenges I have at the current position for which I'm appointed is trying to protect our men and women in uniform against chemical, biological, and nuclear threats so they can protect us and our allies. I spend a good part of my days, nights, and evenings trying to come up with ways in which we can protect the men and women in uniform, whether that be with chemical suits or vaccines, such as anthrax.

Let me just make a few comments, some of which have been made before. First of all, there are a lot more good people in the world than bad people. Unfortunately, there are bad people that want to harm us.

As our legal representative on the Advisory Board indicated, we cannot pass enough rules and laws to stop the bad guys, but we can do things to slow them down a little bit.

One of the things that we observe from natural phenomena, people rob banks because that's where the money is. Those that want to do harm

against using the bioknowledge are going to look where that knowledge is, in the science and technology base and in the companies. So there are things, I believe, we can do to slow the spread of that information down.

That does not mean that we lock up the knowledge. That means we look at some limited distribution. For example, there will be some information that is sensitive enough that we do not want to publish it in the total open literature, and I think as Rajeev had indicated, a lot of this responsibility really comes down at the principal investigator level.

You know, we really need to create an awareness for them on some of the issues that we need to be aware of that people could use in a harmful way, and then that information plus this Advisory Board can help guide us in how we handle certain amounts of information that are sensitive that can really cause us harm.

Thank you.

DR. THOMASSEN: I'd like to just give an example of a different kind of sort of national

security risk from some than have already been mentioned as we've gone around the table. There was an interesting sort of thought piece recently published by former CIA Director James Woolsey and former Secretary of State George Schultz in which they were talking about the opportunities to get freedom in the United States from dependence on foreign oil, and their argument was based on basically two things: one, improving materials so that we could make cars much lighter so that they use much less gasoline; and also increasing the amount of alternative fuels that we develop.

And in the end of their argument, I mean, they claim that the calculations that they and their colleagues have done, that we have it within our capabilities to develop an automobile that would effectively go 1,000 miles on one gallon of gasoline, and that if we could do that, then we wouldn't need any foreign oil at all. We'd have plenty domestically.

Well, one of the interesting corollaries to that in terms of this committee and the science

that's represented here is that if you take the example of converting biomass, specifically cellulose to ethanol, we certainly do that already. I mean it's done around the world, but it's still a fairly expensive process involving heat, involving chemical treatments, and involving biological processes.

And given the diverse almost what seem unlimited capabilities of microbes, it seems well within our grasp to be able to actually design or reengineer microbes or communities of microbes that could do an entire process very cost effectively and very efficiently.

And so one of the interesting, I think, dilemmas we're faced with as a committee, but also as a scientific community is, you know, how far we go in the interest of national security on both ends in terms of limiting or not limiting research or to protect us from harm that could be done, but also to enable us to receive the benefits from that research in things ranging from public health that's been talked about a lot, but also things as different as energy utilization and reliance on foreign sources of

oil.

DR. DIXON: Thank you.

I'm here to share with you this morning the perspectives of the National Institutes of Health on these important discussions we're embarking upon, and Dr. Fauci will be here this afternoon to expand upon these in his discussion.

Let me state from the onset that the NIH is firmly committed to the implementation of the new biosecurity initiatives, and we fully recognize the potential misuse for the new technologies and information that derived from life sciences research.

Yet we do need to put this in the appropriate context and to be sure that any measures implemented are done in the balance that's been discussed by nearly everyone who has spoken, and we do recognize that it's not possible to stop bad things happening from bad people. Yet the goal should be to minimize the risks at which this can be done.

We do support the principle and the practice of a code of conduct in the scientific community, recognizing we need to work together from

the ground up to embark upon this new discovery process in the right way, and that we need to facilitate and develop a culture of responsibility at all levels of the scientific endeavors.

And certainly from the perspective of the NIH, it's important to reiterate the caveat that's been put forward on the need to weigh risks versus benefits.

Consider the mission of the National Institutes of Health to improve the human health, and I think it's clear to everyone who works in life sciences research that there is a direct correlation to the advance of this basic scientific process and the payoff of diagnosis, prevention, and treatment of disease.

And we certainly support that this doesn't pertain to humans alone but extends to the agricultural sector, to animals, animal health, veterinary health, but also to crop animals and to plants for which we depend on for sustenance, and of course, this is of critical importance to the economy of the United States.

So any and all strategies that are put forward, any and all processes need to be considered in the context of the potential risk for impeding the free flow of scientific information and the advance of the very science that could help to bring us solutions through diagnosis, prevention and treatment of the risks that we could take off of the table, and again, to encourage that science is a global endeavor, recognizing that discussions need to be engaged at the international level.

I think it's appropriate to close my comments just in recognizing the efforts of our colleagues and Office of Biotechnology activities and to thank Dr. Patterson and her colleagues for the daunting task of setting the stage and assembling all of the individuals in the time line that they had and to putting it in such a cogent way, and also to thank all of the Board members who have assumed the responsibility and taken up the tasks, as well as all of the participants in today's meetings.

And we certainly appreciate that at the NIH and at the NIAID, in particular, where we've been

endowed with the responsibility of additional resources to pursue the key agents of bioterror, but we're doing this in a way that's placed in the context of the emergence of infectious diseases so that any of the benefits that derive in the smaller circles of the bioterror agents will have benefits and payoff to all infectious diseases overall.

So the processes that you put forward will have a major impact on our processes, and we look forward to working with you and to seeking your guidance as we move forward together.

DR. LUSHNIAK: Thank you for this opportunity to speak.

As we kind of approach kind of looking ahead to the next year, FDA is approaching its centennial celebrations, the last hundred years of dealing with public health issues, and certainly as we look backwards in those hundred years, you look at a variety of public health challenges and solutions that have been made.

Ladies and gentlemen, we have a new public health challenge, and that deals with the issues of

dual purpose research, and I'm confident that looking at the expertise within this group, within the Board itself, that that solution, although difficult to discern at this point in time, will become more clear as we continue to work in this endeavor.

As I mentioned briefly earlier, FDA's mission involves assuring the safety and the security of our food supply, of pharmaceutical and biological agents, and of medical devices.

An important facet also of our counterterrorism mission also deals with the availability of safe and efficacious medical countermeasures, including drugs, vaccines, as well as medical devices and other diagnostic tools.

This mission with its themes of safety, with its themes of security and availability, obviously cannot be achieved without a vigorous and rigorous research program, and this research program is conducted obviously at academic centers, government centers, and also within private industry.

Often this research leads down that winding path termed dual purpose research, and I agree

as we said earlier that dual purpose research or dual use research is really not a binary concept. It's not yes or no. It really is a difficult to delineate spectrum, and the question in front of this Board is, you know, where do we draw the line, and then what do we do about it once that line is drawn.

So I as the FDA rep. certainly look forward to serving as an ex officio member of the NSABB, seek the advice, the guidance, or look forward to looking at the advice, guidance, and leadership regarding biosecurity oversight of dual use research that comes from this Board.

This is obviously a very difficult undertaking, and I'm sure as much of the audience and perhaps the Board members did, we kind of gasped or I gasped a little when I saw the charge put in front of this Board. It's a little overwhelming to look at all of the tasks ahead of us.

Obviously looking at how communication has expanded, we're dealing no longer with just the printed word, but the electronic word. We're also dealing with the internationalism inherent within

research that we already mentioned.

In conclusion, I would also like to tell the Board that you know, the term "ex officio" oftentimes can be a misnomer for people who are just observers, and I would like to stress to the Board that utilize the agencies that are present here. Certainly if there are gaps, if there are gaps in information, if there are gaps in terms of subject matter or other expertise that are necessary for the Board, we certainly saw the qualifications of the Board. We seem to be well covered.

But if something comes up in the working groups, certainly utilize the agencies present here to search out that level of expertise.

Thank you, again, for this opportunity, and I look forward to working with you all.

DR. NICHOLSON: Thank you.

CDC's mission is or vision actually is healthy people in a healthy world, and since diseases know no borders, this applies not only to the United States, but globally.

We have in the National Center for

Infectious Diseases for many, many years great experience in public health preparedness and response. This applies not only to natural infections, but also to those that may be the result of a bioterrorism act.

We have a focus of research that is in the applied areas. That means we are particularly interested in detecting through better diagnostics infectious diseases.

We also are very involved in characterization of infectious diseases, and this has been a long history of us. We have been very interested in identifying sources of natural infections, and of course, that can also be applied in the area of agents of bioterrorism.

We deal with pathogenesis and disease correlates. We have also been, as mentioned here before, interested in environmental microbiology that is from our long history in looking at transmission of infectious diseases in hospital and health care facilities.

We're interested in the ecology, transmission of disease through vectors, and from

animals as well. So we find these areas to be very important, and certainly must continue.

Our focus, therefore, is to protect the public's health. We use various mechanisms in order to deliver our messages not only through scientific publications in peer reviewed literature, but also in the form of MMWRs and other public health messages that go to the public, the health care, and associated communities.

So we're very interested in the Board's activities. We want to insure that there is a balance that includes protecting the health of the public and at the same time protecting information that may do the public harm.

Thank you.

MR. PARKER: Thank you.

I think it's very obvious to everybody here that the Board has an extremely complex, challenging problem, a really daunting challenge, and I just want to maybe emphasize something, a point that was offered up very early in these discussions that is perhaps an opportunity to help us come to some

solutions.

That's really, I think, defined by perhaps our cultures, of our disciplines that we come from here, our multidisciplinary approach, and also the operational backgrounds that are, in fact, represented on the Board and the ex officio members and the active participation I know the Board will get as we move forward.

That culture really represents culture from the life sciences/biology community, intelligence community, law enforcement community, medicine, public health, and an operational first responder community broadly defined.

These communities have got and are coming together like never before, and it doesn't mean that we from our individual perspectives and frameworks and our cultures that we coming to the table to. We don't give up our culture. That's our strength. But I think we have now the opportunity to begin to inculcate some of our different cultures so that we can make sure that we maintain the scientific engine and keep the race up, but also be able to instill the

appropriate security culture necessary to make sure that we don't give our adversaries information that could be used to, in fact, attack our vulnerabilities.

Within the Department of Homeland Security, we actually find ourself most often at the nexus of all of these different cultures, whether it's working with the medical public health community, working with the intelligence and law enforcement, and the operational first user communities, and so I think the culture that we bring to the table, the partnerships represented at the federal level, represented by all of the ex officio members here, but we also have to make sure we inculcate and bring in the state, local officials, academia, private sector.

This is our opportunity to really begin to address these problems. That's perhaps part of the solution to help us think through these tough issues and help us with the response.

Within the Department of Homeland Security, just briefly, some of our biocountermeasures programs. They span from detection, attack warnings, surveillance, response and recovery programs, to

working very closely with USDA in protecting its high consequence foreign animal diseases to having programs that will help us better understand the threat, how adversaries, in fact, might use a pathogen as a weapon to attack us, and finally, bioforensics programs so that we can work with the lead federal law enforcement agency to identify the perpetrator if we are attacked.

So we are very anxious to work very closely with the NSABB, and I also want to emphasize the urgency and the challenge, and I look forward personally to working very closely with everybody on this Board.

Thank you.

MR. KEARNEY: Mr. Chairman, I find myself in the dubious position of being the last of 38 speakers this morning, and as a result not only has my thunder been complete stolen, but the clouds are gone and the sun is shining.

Nevertheless, I'll try to spend just a quick moment reinforcing a thought from the Department of the Interior.

Being a Department of Interior

representative, of course, my eyes are on America's natural systems, and it's not hard for me to imagine a scenario whereby some foreign animal pathogen or a genetically modified native organism has been released either inadvertently or maliciously into America's natural systems.

That would wreak havoc with our native biotic communities and create some catastrophic cascade effects and reduce the resiliency of the ecosystems and impact their ability to provide essential goods and services to the American people.

This would have some very significant economic, political and social consequences. So my point here is that a disease would not necessarily have to be zoonotic and have a direct impact upon the human population, but could be restricted to the animal populations themselves and yet have indirect impacts upon the human populations.

So what are we in the federal government doing about this? Across the different departments we are seeking to develop integrated and coordinated networks of disease surveillance across the human

captive animal and free ranging wildlife communities. We are developing and testing a rapid response capability to identify, characterize, isolate and reduce the emergence of disease be it in human populations, captive animals, or in wildlife.

And, lastly, we're seeking to establish and utilize a system of information exchange across these components of the surveillance and response networks.

What are the overarching themes from this response? Well, the need to think broadly across multiple scales be they spatial, temporal or biological, and also the need to break down organizational barriers among the different components of the systems I've just described to you.

This need to break down barriers to increase communications and to improve information flow is in a tension with some of the things that we've discussed here today. I'm looking forward to working with this community to find the right way to create the communications and to insure that we do this thing right on behalf of the American people.

Thank you.

CHAIRPERSON KASPER: Well, thank you, and thank you, everyone, for your comments.

It's clear to me that there's a lot of wisdom and knowledge in this group, and also there's not hesitancy to share your ideas. I think we're going to have some very vigorous and open discussions about these very important issues.

Dr. Amy Patterson, who is the Director of the NIH Office of Biotechnology Activities, has a few comments to make.

DR. PATTERSON: Thank you, Dr. Kasper.

I was asked to clarify an issue that came up during the break, questions from a couple of the Board members and also members of the audience, and I'll be brief, but I wanted to begin my explanation by echoing the comment that many of the speakers have made that scientific progress is a precious resource, and it's one that NIH, my agency, and many of the agencies represented here today are charged with sustaining and, indeed, cultivating.

That progress, however, is predicated not

only upon scientific talent, but also upon public trust, and public trust itself is a precious resource, one that is earned or merited and enhanced by public awareness and understanding.

It's the public that has provided the support for much of the research that the Board will be looking at. It's the public that will bear the consequences of the federal policies that emerge as a result of this Board's deliberations. For this reason, we want to be exceptionally clear that the Board will meet publicly in accordance with the Federal Advisory Committee Act. On the rare occasion if it arises that we need to close the Board meeting, that would only be done in accordance with the applicable laws and regulations.

I just want to be very clear that this is an open, transparent process, and we think that's a very important aspect of how this Board will work.

Thank you.

CHAIRPERSON KASPER: Thank you.

Well, this concludes our agenda for the morning. We're going to take a lunch break now. All

of the Board members including the ex officios are asked to meet in the Cartier Tiffany Salon, and we'll hear about the Federal Advisory Committee Act and related ethical rules that we must abide by as Board members.

We'll reconvene promptly at 1:00 p.m. for the afternoon session.

Thank you.

(Whereupon, at 11:46 a.m., the meeting was recessed for lunch, to reconvene at 1:00 p.m., the same day.)

A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

(1:20 p.m.)

DR. KEIM: (Banging gavel.) I've always wanted to do that.

Welcome back. I hope everybody enjoyed your lunch. As Dr. Kasper mentioned earlier today, my name is Paul Keim, and I will be chairing the sessions this afternoon. Dr. Kasper had a conflict that he had to attend to this afternoon.

We're privileged to have a variety of experts with us this afternoon to provide an introduction to topics that the NSABB Board has been charged to address. The objective of our first session is to discuss items relevant to the development of the criteria for identifying dual use research and research results.

Please keep in mind that the Board members will have an opportunity to address the speakers during the panel discussion following the last talk. So you can hold your questions.

There's also time reserved for public comment at the end of the day's lecture.

Our first speaker today is an NSABB Board member, Dr. Arturo Casadevall from Albert Einstein College of Medicine who will introduce the issues relevant to the development of dual use research criteria.

Dr. Casadevall.

DR. CASADEVALL: Thank you, Dr. Keim. Thank you, Tom and the committee, for inviting me to present some thoughts.

I thought I would talk about microbes as weapons. Is there a line on the sand? And I began by showing you my car, and I'm reminded about the dual use technology, and I would argue that the civilian passenger sedan is the most effective weapon of war in Iraq, and certainly I see it loaded with explosives. It is easier to make a car bomb than to make certainly Bacillus anthracis in a weapon form.

If you look at the dictionary, a weapon is something, is a club, knife, or gun used to injure, defeat or destroy, a means of contending against one another. And as humans one of the things that history teaches us is that we have used many agents as

weapons. We have weapons that are kinetic, radiologic, nuclear, chemical, electronic, informatic.

And some of your other weapon types are limited by physical laws, and then we are confronted with biological weapons, and here we have the problem that the variety is enormous. The efficacy of such weapons is dependent on both the microbe and the host, and many of the interrelationships are not understood.

So if you even begin to think about the line on the sand, you are confronted with a great gulf in the absence of knowledge.

You can look at missions or weapons as microbes. I'd like to think that there are two ways to look at it. One of them is sort of tunnel vision, and the other one is a tunnel myopic vision. The tunnel vision is a clear vision in that it sees things as either weapon or not weapon, and when you begin to think that way, that has been used, for example, to generate a Select Agents list.

The other vision in which if you are myopic like me and if I take my glasses off, then everything becomes blurry; you have more of a tunnel

myopic vision in which microbes are either very bad, somewhat bad, not so bad, or not bad.

And then the question is: what does this mean? Where does the red go?

And I give you an example. You can buy this at my supermarket, Saccharomyces cerevisiae. So I ask you: is this dangerous? Is this a weapon?

I would agree with you that it is not too dangerous. However, for this individual with AIDS, they got a Saccharomyces cerevisiae related disease, and you say, well, that person is immunocompromised, but already you think about it. In order to define it, you have to begin to think about the host. You can't do it on the microbe alone.

And then you look at the fact that normal women can get Saccharomyces herpes vaginitis. So now you're dealing with a host that is significantly intact, and here is a recent case report about a banker who ended up having a piece of lung taken out because he had a nodule similar to what appeared to be tuberculosis.

So the point is that, yes, you're dealing

with an organism with low intrinsic potential to be a weapon, but then, again, depending on the host this could injure you, and when it comes to injury, you could argue that disease may not necessarily from the individual's point of view, may not be different whether you're very sick from Saccharomyces cerevisiae or from an agent on the Select Agent's list.

You can think the same way of yogurt. Is there a weapon here? Certainly, Lactobacillus acidophilus, depending on the host, can cause severe disease.

So a few years ago we began to think about this, and in fact, select this assignment and not being involved in this and reading on it, I began to wonder how, you know, these agents ended up, and I will add here that I think that our government officials who have generated this list and have done so rapidly have done a terrific job because practically everything that is in there has a great danger to it.

And it has also been done in the absence of a lot of detailed knowledge that has been -- people

have had to have the best guess, and it was done with the emphasis we're trying to protect. So one of the ways in which things ended up in the select list is by historical use. Was it used by the military? Did it cause a pandemic in the past or judgment calls?

However, this raised many issues. It is certainly not suitable for new agents. Many microbes happened to be excluded. For example, influenza virus, which in 1918 killed 80 million people; Neisseria meningitis, Group A Streptococcus; it doesn't appear to be based, at least not from first hand from what you read, on microbial pathogenesis, but I'm sure it is because the individuals who drew up this list happen to know a lot about microbial pathogenesis.

One problem is that it's fixed in time, and it is often species based, and that is too broad. For example, Bacillus anthracis is on the list. Now, some strains, they are vaccine strains and not very pathogenic. Yet they are still considered. So whether you have a non-virulent one or a highly virulent one, it is still the same.

Does it make us safer or more vulnerable? So colleagues of mine are trying to come up with a way of quantitating the weapon potential on microbes, and we made a few assumptions, that each microbe has some weapon potential, and the weapon potential is the function of variables that determine microbial pathogenesis and that this is potentially quantifiable, and here you had the problem that you can't define it from the microbe alone. You've got to be thinking of the host, too. So you need to have a theory of microbial pathogenesis that takes into account the contributions of the microbe and the host, and for this, the kind of visual disturbances we use to damage response framework, which is something we proposed several years ago in which it basically looked at the problem only as an interaction between a microbe and a host.

And it is based on there are three basic tenets, which these are obviously incontrovertible, that you have to have two entities. You cannot define an agent as a weapon from one and alone. Particularly if the host is resistant and have been immunized, it

doesn't really matter. The microbe is not likely to cause disease.

The relevant outcome is host damage, and the damage can come from the host, the microbe or both. There is some sort of function that will define this, and when you go to the textbook and you begin reading or before I show you the function, just to point out if you look at damage as a function of the host response, there will be some mathematical function that will fit the interaction, and if you look at it as a function of time, you will have to state the host-microbe interaction: infection, colonization, resistance, or disease.

The basic relationship for the damage response framework is a problem, and what you see is that for most microbes that cause disease damage tends to occur at the extremes. You tend to have a lot of host damage when there's a very weak immune system or when there is a very strong immune system where the damage is coming from the host, and what you really want is to be somewhere in the middle, and I think here microbial pathogenesis could help us even on the

work of this committee.

You could drag the curb below, and you can see how negative damage is a benefit, and this could easily incorporate those organisms that are known as commensals.

Now, if you look at bioweapons when looked from the view of the damage response framework, what weapon you want is damage all across the entire spectrum, and you also would like, because generally bad people want a bang effect, the damage is rapid as a function of time.

So biological weapons tend to cause a lot of damage in a short time, and when you look at the Select Agents list, you find that by and large, most of them do this.

So we wanted to generate a weapon potential relationship, and we thought that weapon potential had to be based on where a microbial pathogenesis. It had to be somehow functionally within the technological capacity of the aggressor, and then he needs to have human elements, a human behavior, panic, et cetera.

And initially we have dealt only with this part because the other parts are considered amplification factors and, again, the thought being that we wanted to come up with with something eventually that would allow us to put a relative measure or increase damage with a shorter time.

Now, to do that we needed to work at a very definition for virulence, and we defined virulence a few years ago as the relative capacity of a microbe to cause damage in a host. It's a nice academic definition, but it doesn't really help you on ranking microbes.

So we come up with a quantitative one which is the virulence weapon potential is a fraction symptomatic over the inoculum. So you can now see that organisms where they cause disease of very low inoculum are going to appear to have a great degree of virulence.

Now, this is in your slide and it has been published, but the bottom line is that the weapon potential of a microbe is influenced by the inherent virulence of the microbe, the communicability, the

stability, and the time. And the time could be set equal to one if the aggressor is willing to wait forever.

If you now put this set of these variables to the maximum, you could have at least in the scale a weapon potential maximum of 100. So we set out to do some sample calculations by taking data from the literature, and I will tell you that one of the things that is immediately apparent is that we lack the basic information to make weapon potential calculations even with this very simple type of relationship for most of the agents that are already known to be pathogenic. We don't really know the inoculum that is necessary to cause disease. We have only guesses of our stability, et cetera. So basically taking numbers from the literature, taking numbers from monkey studies, assuming no communicability, assuming extreme hardness and the time to disease, you end up with 5.6 times ten to the negative four out of a possible 100.

We then play with other organisms, and you can see that Variola is about 100-fold greater by this scale, and Candida albicans, which is a fungal that is

a human commensal, is very, very low. It's much lower, but it is not zero.

Now, one interesting thing is HIV. HIV is not on the list. However, anyone who knows about what is happening in Africa can see that this organism is essentially depopulating certain areas of the continent. It is almost equivalent, if you think about it, almost a strategic weapon.

We played with it, and if you take the element of time, it doesn't score very high, but if you forget about time, it is significantly high in terms of its weapon potential.

We used it to estimate the weapon potential of SARS, and as you can see, it came significantly high.

Now, one point that I want to convey is the deliverability and immunity change of weapon potential over time. So none of these cases are fixed. If you think back to when the germ theory of disease was first accepted at the end of the 19th of Century, beginning of the 20th Century and you look at some of the developments of the 20th Century in vitro

viral cultures introduced around 1950, the molecular biology revolution in 1970, this is the time of the Cold War.

Bacillus anthracis, for example, was not a biological weapon in 1890 because the technology was not there for weaponizing it. By '45 it was, and in 2004 it is.

For example, the viruses would not have been there because they could not have been grown. They could be grown now.

Now, you could begin to think and extrapolate into the future, and you could ask the question will these agents that are on the list are going to be biological weapons in 2020. If you were to vaccinate everyone with a high effective vaccine against Bacillus anthracis, then it loses its weapon potential.

Variola was probably not a major biological weapon in 1945-1950 at a time of universal vaccination because everyone was vaccinated, and it raises the question: what happens with organisms in which we were very successful, such as polio virus and

measles virus?

As we eradicate them, will they be biological weapons in 2020, that is, if you stop vaccinating because you have succeeded in eradicating the microbe?

So my last slide, some closing personal thoughts, all pathogenic microbes are potential weapons in some manner, and you may have to do something to them. For example, Saccharomyces. To convert Saccharomyces cerevisiae to a biological weapon, but I would say to you, you have to also do something to Bacillus anthracis, and in which case the weapon potential is a function of susceptibility of the population, the inoculum, the technology, and the decision to draw the line is political, and I mean political in the good sense. It is political in the sense of the politics of having deliberate people think through as to where they're going to draw the line, but it is not going to be like tunnel vision where you're going to be able to say this is a disease.

The placing of microbes into various

places may itself be an act of dual use, and you can protect or harm humanity. I believe the regulations that inhibit research make society and make us, the entire planet, more vulnerable.

The weapon potential of a microbe changes with time. Public health successes create weapons, for example, small pox, and the same thing may happen to measles and polio virus, weapons of tomorrow.

So what we mean is that the line in the sand cannot be fixed for the sands shift with time. You need to have some monitoring systems in place, and I think great advances have yielded a lot of great things and to all of those individuals who have labored to come up with a list and to try to understand the threat of the present, but we need to begin to think past that because a lot of the threats are probably out there.

And I said to you that the damaged framework can be used not only for thinking about microbial pathogenesis, but perhaps microbial pathogenesis can give us a hint on how to approach the work of this committee, and you can see this slide.

You could have societal damage, and you could have anarchy on one line or you could have a police state.

And I would argue that damage occurs at both ends, and what you want to do is try to find through discourse, interaction, research some way in which you limit it down here, with the realization that this may never ever get to the bottom.

thank you.

DR. KEIM: Thank you, Arturo.

Our second presentation will be given by Dr. Ron Atlas. Dr. Atlas is the graduate dean, Professor of Biology and Co-director of the Center for the Deterrence of Biowarfare and Bioterrorism at the University of Louisville.

He was a member of the National Research Council's Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology, and he will discuss his perspective on the experiments of concern that were outlined in that committee's report entitled "Biotechnology Research in an Age of Terrorism," otherwise known to most of us as the Fink report.

Dr. Atlas.

DR. ATLAS: Thank you, Paul, and thank you to the committee for the opportunity to present to you, I guess, my own views on what we collectively did in the Fink Committee, the committee that, in fact, led to your existence in meeting today.

I'm going to address the criteria that we used and the system of architecture that we proposed leading to the NSABB. The report that's referred to and which presumably everybody in the room has read and memorized and will quiz me on is called "Biotechnology Research in an Age of Terrorism."

There were points where we had words like "dual use" in the title and we had other things at points, but this is what we, in fact, wound up with in the committee.

I think that as a starting point, I want to give you two very different perspectives on how one would look at dual use. The first which I'd argue dominated many of the international discussions of the Biological Weapons Convention that did not result in a verification protocol had to do with the concept of

dual use as someone trying to do something bad, but hiding it behind a legitimate activity. So you really had a biological weapons facility. You were trying to grow large amounts of anthrax to do harm, but you said, "I have a vaccine production facility. So I can hide it behind that," or, "I have some other sort of facility."

I would argue that is not what the Fink Committee dealt with. Rather, what we dealt with was the activities that those of us in the scientific community carry out every day, legitimate activities, and the potential for subversion of those activities who in the terms of dual use would, in fact, seek to do harm with the legitimate activities and the legitimate beneficial knowledge base that we are trying to generate.

And it was really in that latter vein of trying to limit the potential for subversion that we proposed the architecture that involves the NSABB. In fact, what we, in my view, did was to try to help protect the life sciences so that when we hear claims that regulation or the formation of the NSABB or the

involvement of government, in fact, is harmful to the life sciences research endeavor, I would argue what we were trying to propose was a system to protect it and to maintain the public trust upon which science, in fact, depends.

And what we said was at a number of stages we within the scientific community would look at what we're doing and try to judge the potential for the misapplication of the knowledge we proposed to generate and that we might ourselves then as responsible citizens define some limits on knowledge.

Now, that's appalling to some of my colleagues who say that science is value neutral, that all knowledge has no value good or evil, and that, therefore, there should be no consideration given whatsoever to limiting something.

I would argue that the very prohibitions of the Biological Weapons Convention that says one should not develop biological weapons and stockpile those weapons, in fact, already accepts at the international level with the U.S. as a signatory the concept that there are certain things we just will not

do, and I go from there.

We then define seven classes of experiments of concern, and those are shown here. They are different than the approach that was discussed in the last presentation in that these are process based. They are not based on Select Agents or trying to define an organism that would be a weapon and trying to limit our research or in any way constrain research with anthrax or small pox or other things.

Rather, it was based in part on the original NIH Recombinant Guidelines, which began to say there were certain types of experiments that we'd be concerned about, and one of the ones in the original recombinant guidelines was that if you had a therapeutically useful antimicrobic, you would not use recombinant DNA technology, but have an organism that, in fact, would circumvent that because that organism would potentially be dangerous.

We extended that to vaccines and then we looked at virulence and transmissibility and host range and detection, and then finally weaponization.

Now, I think that this list has at points been misinterpreted. We in no way said that these were experiments that should not be done. Rather what we were saying, if we're going to have a system of oversight that looks at all of the life sciences and says where might danger be, is there any place albeit very limited that we would constrain what we in the scientific community would either ask in the way of a research question or make publicly known to one and all. Which rocks would you look under?

And what we say almost two years ago now was that at that point in time these were the seven places where we would look for. We were, I think, quite clear in saying this was not going to be a static list; that the NSABB would be charged with continuously looking at this list and updating.

I would share with you that during the deliberations of the committee there were individuals who said there are no rocks to look under. Everything is okay. And there were others who brought doom and gloom to the committee, particularly with the knowledge base of genomes and the human genome and

various pathogens and their genomes, and the committee rejected those alarmist calls or viewed them as alarmist at that point and said that really right now, okay, two years ago, the concern was with microbial pathogens. It was with microbes as biologic weapons. It was not with direct attacks.

Now, we did foresee that in the future you would have to deal with the possibility of vectors that would introduce genomes directly into human populations that might alter our moods, our behaviors, our survival, whatever one might think of in that vein. We were not prepared to put that on the list at that point. We restricted it to the potential of microbes as weapons, and all we said was if you're looking at the whole universe, everywhere in this room, and you want to have this Board and have IBCs and others ask questions, ask first to sort of check the box, one of these seven categories, and then have a discussion about it, and the discussion would result in some judgment within the community as to whether there was a clear and imminent danger.

Was this, in fact, likely to cause more

harm than good? And we left it at a very granular level with the hope that this Board would then provide all of the guidance that we would need in the scientific community to know where we were going.

So I've been quoted often in the press as saying I've been waiting for you to come on board and help us understand really where within this list and where else we would go.

One of the things you don't say on this list, that we, frankly, did not anticipate, but it is the news item of the week this week, were studies on vulnerability. That is, we pictured biotechnology in terms of someone actually going to the laboratory carrying out a life sciences experiment and looking to generate knowledge.

We were not picturing someone sitting back and saying in mathematical, scientific sense or otherwise here's where harm might come, and so we avoided, if you will, a category that you're going to have to think about, and that is how close to a road map do some other sorts of non-laboratory studies go.

As I say, these were experiments in the

near term. You now would need to think in the longer term, in my view. We knew these would change as advances in technology. We've already seen significant advances. You already have more things to deal with, and again, these were process rather than organism based, and that was a conscious decision on the part of the committee, in my view.

Again, we didn't propose any sort of ban on these. Rather, it was a filter. It was a simple way of looking at the world and trying to reduce the complexity to something that IBCs might, in fact, be able to do. I hope you can provide the additional guidance that we need.

Thank you.

DR. KEIM: Thanks, Ron.

So our next speaker will be Dr. David Franz. Dr. Franz is a member of the NRC's Fink Report Committee as well, and is also a member of the NSABB. He is Vice President and Chief Biological Scientist of the Midwest Research Institute, Director of the National Agricultural Biosecurity Center at Kansas State University, and Deputy Director of the Center

for Emergency Care and Disaster Preparedness at the University of Alabama at Birmingham.

Dr. Franz will talk about parameters for defining dual use research.

Dr. Franz.

DR. FRANZ: Thanks a lot, Paul.

Well, you'll see, to start with, I changed my title. I agreed to speak on whatever that other title was about three weeks ago, and many of you in the audience know how it's real easy to agree to almost anything three weeks away.

Night before last I looked it up to see what I was supposed to speak on, and I thought it was a little presumptuous of me to be able to provide that kind of information to the committee. So I changed it slightly.

What I would like to talk about is really, David, fighting the last war, but I think it might be useful background for the committee as we move forward. Before I do that, I'd like to just go through two slides that are a perspective of mine that I've developed over a last number of years.

First of all, the difference between biological warfare and bioterrorism, and I mentioned earlier this morning that when I started in this business we were thinking about biological warfare. We were thinking about a cloud of Soviet made bugs coming across the Fulda Gap against our forces in some war with the former Soviet Union.

And there we were facing dual use facilities, equipment and people, difficult problems at that time. It was a tough intelligence target for us to know what was going on in nation-states at that time, and we also lacked real time detection capabilities, which essentially we still lack. We've gotten a lot better than we were, but we still aren't where we are with chemical agents, where if a cloud came into this room, we would have detectors that would tell us in time to put on masks. We're not very close to that. Those are biological warfare problems.

There are also bioterrorism problems, but in addition, in bioterrorism we face the problem of the extremely small footprint of the facility in which target agents might be developed and then of the

agents or the weapons themselves and as we all know, the difficulty with attribution.

I think biological weapons are special, as we've discussed already this morning. Almost anyone could make weapons of some kind, maybe not what we saw in the anthrax letters, but especially when we're talking about highly contagious agents, agricultural agents or in some cases human agents. Almost anyone could do that if they had access to the agents and the will to do so.

The agents will be available in nature. We're not going to outlaw them. The tools are getting better, and our understanding of the tools is getting better. And because of the ubiquity of the tools and the bugs and the fact that they're legal and, a focus of this committee, that they're necessary actually for good, intent, I think, becomes an extremely important part of the equation.

And as the technical barriers have come down and will continue to drop over the next 20 years, I think intent will be an even more important part of the equation.

I mentioned my frame of reference this morning, and here we go back to fighting the last war. Certainly mine is one of military medical biological defense. This is sort of where I grew up in this field, some infectious disease research for the military, and then I was greatly influenced by my time with UNSCOM and the trilaterals, the U.S.-U.K.-Russia agreement in September of '92 to reduce the likelihood that the Russians would continue their program, and then the Nunn-Lugar cooperative threat reduction program that I mentioned as well.

In that context and with that background, I'd like to look briefly at -- and this is a little bit historical -- the dual use nature of people, facilities, and equipment.

First of all, people. When I stood there at Al Kindi (phonetic) veterinary vaccine facility and looked into the eyes of Dr. Rahid Taha, I was wondering if she was a weaponeer at that time, didn't know. I didn't know her intent. She was a scientist trained in the West and in a discipline not unlike mine.

We talked about science. We talked about a lot of common things. It was still difficult to understand intent. At that time I was on that side of the intent barrier.

A couple of years later I was proud to accept the colors of USAMRID. Actually I don't think Ernie is here anymore, but Ernie handed those to the general and the general handed them to me, and it was my laboratory. I was very proud to be the commander.

But then I faced some of the same criticisms, and we in the institute faced some of the criticisms by people who didn't understand or didn't really believe our intent. And I think this is an issue that we will be facing in this country both domestically and internationally, some of our colleagues internationally and some of our scientific colleagues in this country will be concerned in the future with some of the research that we will be doing, defensive research that we'll be doing to protect our citizens.

So it's not always us on one side or the other of that intent equation. I think late '90s I

saw the value, as again I mentioned earlier, of science as a common language, and this is one of the first meetings I attended where there was a combination of many former Soviet Union Warsaw Pact scientists that had been involved in offensive programs, and many of us who had been involved in defensive programs or just in science in the West, and it was here that I first really became aware of the importance of communication, of open discussion, and of working together on common problems if we can.

You can look at these pictures, and it's pretty hard to tell intent there. We all look pretty much alike, don't we?

I was also influenced by Dr. Dave Huxsoll, who was the commander of USAMRID when I first came there, and this was a -- we called it the Huxsoll hairpin or the Huxsoll antibody, I think. When he developed this, it was some of the early thought in the late '80s with regard to dual use. And I know there came a point when we were told not to use this in any of our briefings because it was wrong. I have it here for historical reasons.

But it was good enough for me because I didn't have experience. When I went to Obolensk, the facility up in the upper right-hand corner, Building 1 at Obolensk, one of the former closed Soviet cities, it became very clear to me this concept of dual use or development of certain facilities for the production of biological warfare agents and then others that could go either way.

But this was one that was a real lesson to me when I walked in there. That one didn't look like a vaccine facility to me, especially the suites on the upper floors.

And then in the following years, I have had the opportunity to look at a number of other facilities. Al Hakam in your upper left was pretty hard to tell. That would be very much dual use. It was called a single cell protein facility. If you looked into the science and the production and the actual capabilities, that would be brought into question. But it wasn't nearly as single use as what I had seen in the former Soviet Union.

USAMRID on the right could be considered a

dual use facility. Vector down on the bottom right out in Nova Sabirsk (phonetic) looked less single use to me than Obolensk had and more like what we had seen in Al Hakam. It could kind of go either way, a massive, massive program, but a different kind of a problem.

And now, today, and in the few years to come, the NIAID and other organizations will be funding a lot of containment facilities like the drawing of one we see in the lower left that I will be responsible for when that's completed next August.

Again, a containment facility, BL-3 space, work with human and animal pathogens, and there will always be the issue in facilities of dual use and of intent.

Equipment is another issue. European fermenters that we saw in those facilities at Al Hakam could be used for legitimate purposes or they could be used to grow weapons agents. The enormous facilities that we saw in the former Soviet Union could be used either way.

A fermenter like this could be used to

grow botulinum toxin to make toxoids as this one was here in this country, or it could be used to grow the toxin as a weapons agent.

Other pieces of equipment, an orbital shaker, dual use; freeze dryers, liotholizers, dual use everywhere, in all of these facilities, Iraq, U.S., Russia.

Here, a perfectly legitimate activity in a warm room, growing Clostridium noviae, chauvei, and perfringens vaccine to protect goats and sheep could also be a great facility in which to grow botulinum or other anaerobe.

Then there are the higher levels of containment in which one can work with the filoviruses and the other hemorrhagic fever viruses for good or for ill.

Things as mundane as pure water supplies that you might need for a vaccine facility you might also need for a warfare facility, things like plate and frame filters. I had never heard of one until I started going on these missions and Bill Patrick explained to me that we used them in our old program

to clean up media and also to clean up liquid formulations of agents, very dual use.

The ubiquitous double ended autoclave that we have tens of in this country, but were always an indication of a potential problem when we visited on these inspections.

And then generating aerosols here in a Cullison nebulizer, a Class 3 hood line of listed agents, the Select Agent lists. In this case to make vaccines; it could also be done in order to evaluate biological agents.

Now, this isn't very dual use. This was a Mig refitted with some French Mirage equipment to deliver a liquid slurry of a Bacillus simulant, but this one on an air field that is used for crop dusting could be dual use. You might fly one day one way to spray your wheat fields and fly the other way and modify the nozzles slightly another day to test the release or the dissemination of biological agents.

And actually most of our time on these inspections was like putting together puzzles. What's that? What's that? That looks kind of dangerous. Is

that a dual use item? And that looks like a controller for a fermenter. I wonder what that was used for.

So very difficult problems, and as we've heard from other speakers, there aren't bright lines in these when you're thinking about dual use, whether it is people or whether it is facilities or whether it is equipment.

With this little bit of history, I would add that I really believe that Iraq, the issue we dealt with, issues we dealt with there under UNSCOM and then under IMOVIC (phonetic) later, the former Soviet Union, and really the entire '90s are probably easier and were easier than the kinds of problems we face today for a number of reasons. The bugs are still available. The technologies are getting better and are going to continue to get better.

Our understanding will get better. The terrorist footprint is much smaller, as I mentioned before. It's a much smaller world today. We don't have big oceans and friendly neighbors on the north and south. We still have them, but they don't protect

us like they did before.

And I think as a result, intent becomes even more important.

So when I look at the cost of safety and security, and in this case, as depicted by these pictures, sort of from both sides we have to consider that. I think maybe first about regulation. Can't we control this? There must be a way to make us safer, and then I think about progress and feel, well, if we over regulate, we're going to limit progress, and we absolutely can't afford to do that because, as has already been stated, much more good will come from science than ill.

And I start thinking about intent, as we have mentioned. Perception becomes very important, and when you think about perception, education becomes very important and communication.

And I don't know that Ron mentioned it, but one of the major focuses of our thought on the Fink Committee was this concept of education and awareness and building the kind of culture that was mentioned this morning.

And then finally balance in all of these areas. I think we have to seek that balance as we more forward.

Thank you.

DR. KEIM: Thanks, Dave.

So at this point we'd like to open the floor up to the committee members, both the appointed committee members and the ex officio members, to ask questions concerning these topics, in particular, to the speakers, but also make comments on your own.

Just to get the ball rolling, I will address this to Ron or Dave, in particular, but, Dave, you mentioned, of course, that one of the dual use factors that you were concerned about were people, and while in the days of the bioweapon years this might have been readily definable as somebody worked on a biological weapon for a state.

These days we kind of face a similar issue concerning training of new scientists in the area of, you know, biosafety containment and pathogens, and at least in the case of Selective Agents, people who work with these pathogens have to undergo a Department of

Justice background check these days, and that pretty much eliminates foreign students and foreign post docs from having access to these agents.

I was wondering if you or Ron, since, Ron, you're involved with a lot of educational processes; what's the effect of the current regulations on training of students and experts in our society, and what do you see as the future there?

DR. ATLAS: I guess the answer which I would give and which was used in crafting the Select Agent regulations is that it should have minimal effect. It's a system aimed at developing a basis for trusting those you have in the laboratory, but the Select Agent rule did not eliminate foreign students, postdocs, visiting scholars from participating.

Yes, it required a clearance process, but the only exclusions were aliens from a very limited number of countries which would have essentially no impact on the scientific endeavor.

So I think that it's important to stay with the mandate that the Congress gave in enacting that regulation, which like everything else in this

field is aimed at to the maximum extent possible, we have openness in science, and only in very few, very carefully defined, and very narrowly defined areas do we do anything to constrain that.

DR. KEIM: I guess I would just come back and say that sometimes the intent and then the practice can differ. In the case of the Select Agent Act, my laboratory has had a Select Agent license since the late 1990s. In fact, when we first received our Select Agent license, we were required to pay a fee of $13,000 because Congress hadn't appropriated any money to run the program.

And over those years, my experience with the Select Agent rules has been that, in fact, it does impede or at least slow progress. The question is in the balance of things is that a good thing or a bad thing. And I think that's a bigger question.

In the case of the background checks, in fact, it's often hard to get a background check done on a foreign national just because their records are not as readily available, and so the time line can actually become prohibitive.

So, again, here's an example where we didn't really intend to impede the progress or the interaction of particular people, but the practice of making it work can do so.

DR. LEMON: I have the luxury of working in my laboratory with an agent that's non-select, Hepatitis C, but we have a lot of individuals at UTMB that do work with Select Agents and labs that are registered for that purpose. And one of the effects is with American graduate students going through the various clearances required to get them into the laboratory. It makes it very difficult for them to enter those labs on rotations as graduate students, which provides a disadvantage and a disincentive to faculty to actually work on those agents. It's just an unintended consequence of a well intended regulation that's a little difficult to work through.

We might improve that impediment by a more rapid clearance procedure and so forth, but it has been a real impact.

DR. CASADEVALL: Just to add to the collection of anecdotes, my laboratory works on

developing antibody therapies for Bacillus anthracis, that is, for developing passive therapies and to work with Bacillus anthracis as a Select Agent, you have to have select license.

Now, we don't have that. So we are allowed to work with a vaccine strain, which is a certain strain that has the toxins but doesn't have the capsule.

It turns out that we're allowed to work with that because that's a vaccine strain in the United States, but there are a lot of other attenuated strains in which you have the capsule, but they're not on the United States vaccine list. So we can work with those strains even though they're also attenuated because the Select Agent basically is a species almost kind of a designation.

So consequently a lot of the work simply cannot get done, cannot get done, and it has been done with collaborators and only if I apply for a select license and turn my laboratory into a Select Agent laboratory with all the issues that are involved; this work is severely being hindered.

We have made reagents that we cannot test or not test easily because of the regulations that are in place.

DR. KEIM: Mike.

DR. OSTERHOLM: This is a question for David.

Several times in your slide, you refer to the fact that a terrorist footprint is much smaller. Can you explain what you mean by that?

DR. FRANZ: I just mean the potential for the use of biological agents. For example, what we saw in the letters was much smaller than the four rows of ten, 64,000 liter, 50,000 liter working volumes I showed in one picture or the enormous, enormous program we saw in the Soviet Union in general, and really the fair size program we saw in Iraq.

I think the potential for doing harm in a much smaller facility with a smaller amount of material is there today that we really didn't think about when we were talking about battlefield weapons.

DR. OSTERHOLM: Well, if I could just add a point to that. Is it really the footprint is

smaller or is it the fact that there's much less material and ultimately the delivery system will still determine whether you have a million of something or ten of something. It's how much you can deliver over what time to wherever you're delivering it to that will ultimately determine what the size of that faucet is, and unfortunately today with the kind of delivery systems we have, which have improved dramatically, you can much more efficiently deliver whether it's through air or through food today certain amounts that are much less than one before.

So I guess I would almost call it the kind of economy of scale. We can do a lot more with a lot less today. So a terrorist today could probably have a footprint of substantial proportion today that they couldn't have accomplished 20 years ago before aerosol particle technology or before the global distribution and widespread distribution of various food sources.

So I --

DR. FRANZ: I think we're just using "footprint" in a different way.

DR. OSTERHOLM: Okay, okay. I think it's

one thing to think about the anthrax letters, which was a very valid observation, but think of that same individual or groups instead of using the anthrax spores in letters had just put it in a baggie and walked --

DR. FRANZ: You're talking about the footprint of the aerosol cloud. Yes, and I was thinking about the footprint of the system it takes to cause harm.

DR. OSTERHOLM: I was just thinking if you put that same baggie full of material --

DR. FRANZ: I should have made that more clear.

DR. OSTERHOLM: -- in a building air intake in one of our large skyscrapers, we would have had tens of thousands of cases as opposed to 21 cases.

DR. KEIM: Dennis.

DR. DIXON: Yes. I'd just like to address Arturo's point about the vaccine strains of Bacillus anthracis and the limitations of the species concept.

It does give a good example of what I think we could give credit to the CDC for implementing

in the Select Agent process, and I think it shows a limitation where a lot of the deliberations were done within the government and a lot more took place and was appreciated on the outside.

There is a monthly or less frequent, if not needed, scheduled panel meeting of government experts, the Interagency Select Agent Technical Advisory Working Group, that deals with issues as they arise, and that's the group that helped to create excluded strains of Select Agents.

And this is a data driven process. So individuals can petition CDC and Mark Hemphill who's here in the audience might want to comment on this additionally with the anthrax situation, which is very complicated because it depends on the risks of the vaccine strain being reconstituted to wild type potential, and one of the plasma deficient strains is less of a risk than the other, and the one that we've exempted is less of a risk than the other, and the one that we've exempted is less of a risk.

But there is the possibility in the process for a scientist who go to the CDC point of

contact, Mark's office, to propose data that show that a listed agent when modified in compliance of all of these requirements for working with those agents has lost in a definable way, an irrevertable way the capability to inflict the same damage that it had before, that it can be delisted and made an excluded strain and so characterized.

That's an ongoing process. It is a good point, but it shows that having a data driven, adjust as you go along system is very useful in approaching these issues, not locking in on something in stone.

DR. LEVY: I just had a comment. I was kind of interested in the focus of the three speakers. In a sense, Dr. Casadevall focused on the organism and the fact that we have identified or others have identified particular organisms, but actually any microbe could be turned into a weapon depending on both its pathogenicity traits or, better yet, what we talked about earlier, amplification and an ability to spread.

Dr. Atlas then spoke about the kinds of experiments, seven in which dual purpose may be found,

and I think he was right in saying that if you are purposely creating a weapon, then that isn't really dual purpose. That's single purpose, and it's a purpose we don't want. It's the dual purpose, and often perhaps done innocently, but whose publication might alert someone to a dual use. And I think that that is another aspect of the problem.

But the third I found even more fascinating, and that was Dr. Franz's argument for the intent, and I think that's a much harder aspect. I mean, we are focusing on the organisms. We're focusing on the kind of experiments, but what about the intent?

And looking at your list at the end there of regulation progress intent, I really think that the emphasis should be not on balance, but on education. I think it should be on education and communication.

You know, criminals will be criminals. But unless we can help young students to distinguish between what is really good for the world and what is bad for the world, we're never going to make it because someone can always do something wrong.

So knowing what could be wrong is one thing, but getting the message out not to do it is, I think, one of our best defenses, and I think getting societies worldwide to agree that there are certain criteria for the good science as opposed to bad science that may go a long way in getting a universal acceptance of good science.

DR. KEIM: Dr. Cohen first.

DR. COHEN: Thank you, Paul.

Similarly, I have a question regarding the people aspects. Dave, the question is really for you, but I'd also like Ron to perhaps shed any light that the Fink Committee may have considered in this issue.

My question is people aren't all good or all bad. They also change over time. They're also influenced by circumstances that may have nothing to do with the work, just life as it goes on outside of the laboratory.

So background checks, to whatever extent they might even be effective, do some screening prior to coming into the lab, but in your experience sort of looking into the eyes of these scientists and asking,

"Are you a weaponeer?" do you have any sense of ongoing personnel reliability, any ways or means to screen or to routinely recheck perhaps any changes of intent?

And then, Ron, if you could shed any light on conversations about this that may have come up in the deliberations at NRC, I'd appreciate hearing them.

DR. FRANZ: With regard to your question about personnel reliability or surety, are you talking about history here?

DR. COHEN: No. Someone with a perfectly clean history coming in and working in the lab and over a period of months or years becoming compromised, either psychologically --

DR. FRANZ: And you're asking about Iraq and Russia?

DR. COHEN: No, not in particular. I'm just wondering if you have any experience. The question goes back to the comment that one of the Board members made about background screening and comments that you made also about background checks.

That fixes a point in time. So someone is

brought into a laboratory to work and passes a background check. Two years later that person may be someone who would have reason to or could be found out later to be responsible for sabotage or theft of material in a laboratory, for example.

I'm just wondering if there's any experience you had or if Ron had any presentations of background in deliberations that were made before the NRC committee dealing with ongoing reliability of workers who were otherwise perfectly clean coming into their work, perfectly fine history but over time change.

DR. FRANZ: Right. Well, as you know, this is a new world in biology. Fifteen years ago or 20 years ago, you would go to an ASM meeting with a vial in your pocket probably. At least some people would.

But that same 15 or 20 years ago, we had surety programs in our chemical community, in our nuclear community, and I have not worked in nuclear, but in chemical I have in the military, and that was an ongoing examination. You know, you're looking for

psychological factors and so on in individuals, and my medical records had a great big stamp on the front of them that said I was in a surety program, and I was looked at all the time.

Those kinds of things, as you know, now have moved to biology, and I haven't been involved in that area since they have moved, and I don't know exactly how they have changed. And I think it's primarily in the DOD; is that right? The surety programs are primarily in DOD research, not in any of the other research.

But that in my experience changes the way you do research in that it slows progress a bit, but it has to be done very objectively and very carefully in order to limit progress as much as possible.

So certainly I have had experience in the programs, but not really experience with change in individuals.

DR. KEIM: A comment here first.

DR. IMPERIALE: I guess I have a question for Dave also regarding intent, and that is that assuming that we're dealing with your average, you

know, university laboratory or even industrial laboratory and assuming that there is a code that we all agree on and everyone signs onto, then I wondered how you envision assessing intent and is that really going to be possible or not.

Because a lot of these things may be inadvertent.

DR. FRANZ: I had always hoped DARPA would develop an intent meter that we could put on people's heads, but so far --

(Laughter.)

DR. FRANZ: But anything is possible at DARPA though.

PARTICIPANT: They're working on it.

DR. FRANZ: Okay.

(Laughter.)

DR. FRANZ: But the general approach that I believe was taken before surety, and it might get a little better with surety, but intent, we still won't measure intent, was to work with people for a long time before you take them especially into BL-4 suites. I would say in my laboratory five percent of the

staff got into BL-4 and maybe 20 percent into BL-3. Most people worked in the cold all the time.

I'm just guessing at those numbers. I don't know that that's exactly right, but it's a small number that go into BL-4, and I can think of some of my division chiefs who worked and worked and worked with people side by side for a long time before they would ever let them go in, still not unaccompanied, but with someone else, to be very comfortable.

And you know, that's what it's all about in biology. In nuclear or chemical matters you can have meters or ways of measuring how much is being taken out or how much someone has. In biology it's that much.

And so it depends on people, and that's always going to be a difficult problem, but I think open communication and working close and education, as was mentioned -- I'm a huge supporter of education for this -- and awareness are the way we're going to have to go.

DR. IMPERIALE: So you see more of an issue of trust.

DR. FRANZ: You have to eventually trust, certainly.

DR. KEIM: Dr. Lemon and then Dr. Rubin.

DR. LEMON: Thank you.

I think this is a really important issue, particularly as we gear up to complete construction on a large number of new BSL-4 labs, given the number of individuals that today qualify to work in that environment and the need for a mentoring kind of training experience.

But the comment I wanted to make is to Ron, and actually it's a question. Given the fact that we do live in a global community and that if we're going to succeed in this charge it must be a global success, I wonder if you could comment on the international response to the Fink report.

Has it been noted abroad? And has there been a favorable response or just what has been the response?

DR. ATLAS: I think I've been traveling a great deal internationally talking about the Fink report. I think there's a wait and see attitude.

Internationally I still have the sense that there's real fear of what the U.S. government is doing, and there's a growing fear that the NIAID biodefense programs, in fact, cover for biological weapons programs. And so there's fear of what we're doing.

Within the United States, I'd argue that the real fear is of bioterrorism, of the misuse of the scientific community to do harm, and that we see the NIAID biodefense effort as very beneficial to developing the vaccines, the therapeutics, diagnostics, and all else that we need to offer protection against that threat.

So there's a different global view. From the Fink committee perspective, from day one we saw this as needing global outreach. The model that we used was the recombinant DNA debate, which I would argue for better or worse started in Asilomar with conversation in the United States, but then led to where the OECD and the WHO developed parallel structures so that we began to have a global agreement on the safe conduct of recombinant DNA research.

And the Fink committee was hoping that

this would not be a walled off U.S. effort, but would be a dialogue internationally, and called on us to move forward that way, called on you in the NSABB to move forward that way.

Without that I don't see much value frankly in any of the efforts that we might be conducting.

DR. FRANZ: I would just add to that that the Intentional Epidemics Group at WHO that are in the facility, and I think now Mary Chan is boss, are working on this in collaboration with a number of other countries and are going to do essentially Fink kinds of activities in the seven WHO regions and have plans to do that.

DR. KEIM: Harvey.

DR. RUBIN: Actually Dr. Atlas just touched on it and Dr. Franz mentioned it explicitly, and that's this idea of perception, which is a new dimension that hasn't been mentioned before, and in one of our briefing papers by this fellow Tucker, it refers to federally funded laboratories and the notion that we've been talking mostly from the perspective of

university labs where we basically choose the projects we want to work on.

I wonder, David, if you could comment on research that's now proposed or expanded in some of the new labs that will be stood up either by homeland defense or DOD and the notion of more directed research and how that might be perceived in the community of the United States as well as abroad.

DR. FRANZ: No, I can't comment specifically on what's going on or planned in those labs, but I think your point about perception is important and I know I'm already hearing from people in the media that are concerned about your question exactly, and I think it's something we have to take very seriously.

There's no question in my mind that we have no intent in this country to contravene the Biological Weapons Convention, but there are people who believe we might, and there will be cases where we need to do some classified research, and how do we convince them that it is not contravening the convention.

I think there are concerns domestically, and there are concerns among our international colleagues. I have often said where we can and when possible, if we can collaborate with one of our allies, that might be a way to diffuse some of that internationally and domestically.

Likewise, there might be cases where we can talk about research and explain the research that's ongoing, but maybe not provide the results if it exposes a vulnerability or compromises us in some way. But I think we can't just ignore that issue of perception.

ADM. STUDEMAN: I'd like to comment on the security dimensions and focus on the issue of counterintelligence as an analogue to the question of dealing with people and security.

Obviously in the intelligence community the opposite of intelligence is counterintelligence and security, and we have, of course, very significant processes in place already for clearances for training, for ethics standards, for polygraphs, for financial disclosure, for reinvestigations, for

expedited investigations, paid investigations, a lot of process that relates to the whole security, maintenance of security.

And the fact of the matter is the history of espionage has been that at any given time there are probably two or three bad apples in the system, if not more, and that the insider threat is the largest threat. The outsider threat clearly is a significant threat, but the insider threat is the threat where the most amount of damage takes place.

So I think the message out of that is that you have to have all of these things, training, ethics, standards, process, et cetera, investigations, clearances. It's probably a necessary but not a sufficient condition. One could probably question whether the cost of it in both process and actually in dollar value justifies, you know, the gain that you get out of it, but I suspect there's nothing to replace it now at this particular point.

I think the one thing that we have learned though from the espionage analogue is that good offense as well as good defense is an important

dimension to this.

By that I mean casting your net widely and, in fact, penetrating hostile intelligence services that are working against you. In the case of our case study, we would be dealing with whoever the threat agent is.

So focusing on the threat agent and the connection between the threat agent and the insider, presuming the insider is not operating on his own, is a very critical dimension here.

DR. ERLICK: Kind of to draw the discussion a little bit back to the technical issues, it strikes me that we're talking about a whole -- what shall I call it? -- heterogeneous cascade of efforts because we start with fundamental research and then as the discussion went, we moved on to the actual production methodologies, and then interestingly, weaponization, primarily aerosol technologies, et cetera.

And I wonder if I could get -- Dave, maybe you could speak to this -- in terms of our charter and what we're looking at, it seems that we're looking at

more of a global issue than anyone would suspect when they first hear that we're dealing with biosecurity. You would think we're talking about research in the laboratory, but in fact, we may be getting into the pesticide industry and areas like that that incorporate biologicals.

Dave, what do you think about that? The scope is maybe a little bit broader than your first thought?

DR. FRANZ: Well, I think so, and I think I heard that in comments from a number of the committee members as we went around the room this morning. I think, and someone else may have a better perspective on it than I do, but I think it's very, very broad. You know, it's a moving target as was mentioned.

As technology changes, it could be exploited. There may be areas that we don't understand yet that could be exploited at some point or accidentally used.

DR. ERLICK: Again, my comment. It strikes me that it seems our worry meter is quite

significant because we're concerned about genomics, which have their own set of problems, all the way to fundamental delivery systems. So it seems to be more than fundamental research in terms of just biological, but I'm wondering -- and it kind of makes me think about getting into the engineering aspects that are related because if we look at the agent as the fill for the actual weapon itself, the weapon, in fact, may be a cold fogger or whatever, but it seems like we should worry about everything in toto rather than just simply how do you alter the agent to make it effective.

It may be that we're looking at experimentation for a more efficient dissemination process also.

DR. CASADEVALL: Well, to follow up on that excellent comment, I mean, you have to think that the Bacillus anthracis, attacks in 2001, uses the delivery, our mail system. That was the delivery agent, the envelope.

DR. RUBIN: I just want to expand on that a little bit and see where it takes us if we just keep

reducing it, and this is a question for you, Arturo, because it looks like you were trying to do some mathematics, and I always appreciate that. I think that's great.

The question is, I mean, models aside, there's a lot of effort now to do mathematical modeling of outbreaks and mathematical modeling of this or that, and the question is: does that start becoming a Select Agent? Does one's model become a Select Agent? And where do you draw the line in terms of the mathematics, in terms of the algorithms?

You obviously have your algorithm that you developed. Do you think that becomes part of our charge as well?

DR. CASADEVALL: I think it is part of our charge to discuss it. But I would say to you that I guess anything that you do in this area is to potentially dual use. You could argue, and we thought about this, I mean, if you begin playing with an algorithm, could somebody use an algorithm to then figure out what a biological weapon would be.

And the way that I reconcile myself that

that was not going to happen was when I began to try to do the calculation for Bacillus anthracis and realize that the data was not there so that it was, in fact, more important to alert people that if you're going to evaluate the weapon potential of Neisseria meningitis or something like that, you may not, in fact, have the variables.

And that provides you with an opportunity, I think, for protection because the exercise shows you what you need to do and shows you what your liabilities are and your vulnerabilities.

DR. OSTERHOLM: I think just to follow up on that, this is a very critical point because I think far too often we look at biosecurity and agents as a laboratory based function. To me this is a lot like cooking a souffle. You can either somehow invent a much better egg that gives you a much better souffle, or you can get a much better skillet that cooks it much better, which is the means transmitted in a sense, or you can basically give away a heck of a recipe, which is basically the how to do it all and all put together.

And today we have to worry about all three. We have to worry about can we make a better bug; can we disseminate it much better; or do we have informatics today that allow us to basically take that whole recipe and now make it readily available to somebody who otherwise wouldn't have had all of the pieces to put together, but could get the component parts.

And I think that that's the recent week's discussion over the paper that appeared relative to Bot. toxin in milk that was recently referred to this morning. Does that meet that third standard of now making it much more available to someone who might otherwise put it all together?

And I think our purview really has to include all three of those issues because in a sense, as you pointed out very nicely, the equation on the bug and so forth is partly bug delivery and all the information.

DR. RUBIN: So you recognize that. I think that was the paper an economist, and in our place there are engineers working on these kinds of

issues, people at the Wharton School doing computational analysis on vulnerability of networks.

So we're now going to have people in the Wharton School applying to the IBC to do that kind of work. I mean, so the reach of this committee is becoming, you know, octapusoidal.

(Laughter.)

DR. RUBIN: It really seems that we may have to think about drawing boundaries somewhere or else we'll be here forever, even though we were totally wrongly for four years.

DR. OSTERHOLM: Well, I don't think my comments was meant to suggest that. My comment was around biologic agents, first of all,

Second of all, it was pretty much around the issue of both the agent and the millions who transmit that agent in a more efficient way. I mean, one of the things we forget is technology is not just around growing bugs. Technology is how to deliver them.

Aerosol particle technology has improved dramatically in the last two decades to the point

where today I can go out and buy devices at various electronic shops that only in yester year would have been available to the bioweaponeers in the highest levels of government programs, and so part of it is that we have to understand that it's the combination.

But the third piece which is key is not just computational. I don't want to suggest it's all things, but if you give somebody now where is the important node, where does it get by, a good example -- let me just use this from the food standpoint -- for the last 15 years in this world, we have basically approached food safety from the standpoint of what we call hazard analysis of critical control points, where we go into the food system and try to figure out where are all of the vulnerable nodes that Mother Nature might, in fact, create a food problem.

Today those very plans are the very blueprint for a food terrorist because now they know everything in the system that we have to take care of Mother Nature, and if we get past that last block and now you can do it, you're home free.

And so in a case like that, by taking that

plan and putting that together in the right setting, you literally give somebody a step-by-step blow of how to do it, and I think that's one of the things we have to also consider. Does that information now become also a critical piece of biosecurity, safety, and I would say both prevention and response?

DR. ATLAS: And just to add the question of the engineering, I think that my perspective would be that the closer you come to a true delivery system, the closer you come to a real road map. That's where you get most concern because it becomes a clear and imminent danger.

I think that you may debate for a long time on the fundamental knowledge side, the genomes, the sequences. In the end you can point that as technology advances, as knowledge base advances, risks will be there. Accept that. That's going to be the case.

I don't think that you can constrain that or you should consider constraining that because that's really the basis on which we advance the science. The question is when you get towards

development, if you look at the Biological Weapons Convention really starts at the level of development, well when does research really get real close to development; when is it a road map; when is it a technology that is clear and imminent in its danger?

I think that's really where you're going to find yourselves being driven. At least that's where I've been driven in much of my consideration.

DR. KEIM: So David first.

DR. RELMAN: I like the concept of looking at vulnerabilities as a metric for understanding where unusual risk may exist. But vulnerabilities of course also reveal points of intense need for further work, and we all recognize that a flexible, agile scientific enterprise that understands where there are important needs for research is one that will help us get to where we need to be more quickly.

Perhaps we can elaborate upon the idea of focusing on vulnerabilities and look at situations in which vulnerabilities are also accompanied by untoward gaps in time before which we'll have any suitable defense, as a place where there is special

vulnerabilities and places where we might really focus our efforts.

The idea of identifying maps or road maps is a tough one because many fundamentally important papers in mechanisms behind virulence are, in fact, blueprints for constructing strains or biological agents of potential untoward effect.

So I think that does get back to intent sometimes, and emphasizes the importance of looking at vulnerabilities and what we might be able to learn from that circumstance that helps us understand where those few places are where the gray turns dark.

DR. LEVY: I guess I'd like to be reassured that good science that can help us in the area of infectious diseases will not be destroyed because of a fear that it will end up to be a road map. I think what Arturo told us this afternoon and Dr. Lemon mentioned this morning is that we need a lot more research to understand how infectious disease microbes move.

I mean, it's pretty obvious that even particular disease agents that we've identified or

newly identified ones, the sooner we know how they're transmitted, the speed and by what route, the faster we can move to eliminate their spread.

So I would move very strongly towards increasing research on disease spread of which we really only know very little, a little bit in the hospital, a little bit of hand washing, but I would hope that there would be more effort in that regard and not worry about whether that would open up some area, a new area, a new road map, another dual use.

And I'd like to have your comments on that, Arturo. How do you feel? You did that research and you found there wasn't much information.

DR. CASADEVALL: I mean, I think so, and I would also point out that the benefits that accrue are often very difficult to rationalize. For example, there are research efforts that look at anthrax toxins in the treatment of cancer. So even defense research that is what appears to be bioscience related may -- or in some ways military related -- may have tremendous payoffs in the non-defense arena.

And I will ask you to think about a lot of

the technological advances of the 20th Century and to the degree in which they were further along by, in fact, some of the thoughts that were or some of the developments that were used, for example, the jet engine, satellites, some of the micro electronics.

So it is conceivable that as money is spent in infectious diseases and in particular, in basic research in infectious diseases, that you will also see bonanzas in areas that you would not necessarily expect right now.

DR. KEIM: I've just been reminded that this committee is, in fact, supposed to provide guidance and leadership regarding biosecurity oversight of dual use research, and so much of our discussion is starting to move away from research alone, but just a quick reminder about that.

DR. ERLICK: I will make a comment, and I agree 100 percent with what Stu is saying about research, and it reminds me of the arguments that have been going on the last decade regarding Variola major where there was a strong sense that we should destroy it because we had mapped it and everything was okay,

and I think that has quieted down now, that it presents itself as a significant threat agent, and we found out we don't know as much about it as we thought we did. So that's kind of the argument made.

We may think we're very, very bright right now. We know a whole lot about disease mechanisms and causative agents only to find out later on that we've maybe taken a position that was too strong to eliminate a type of research or line of research or in this case a particular agent, and in fact, once it's gone, it's gone.

So I would argue that we need to go very, very softly in terms of trying to make recommendations to regulate research and think it through a lot.

DR. KEIM: I'd like to come back to a point that Mike Osterholm was making a moment ago.

Mike, you were talking about, in fact, the threat is really a multiple stage thing in which you have to have all components. Is it possible to define key components and that, in fact, we can deem these key components as safety valves and so we can work up until that point?

I mean, the analogy would be that the Select Agent rule, in fact, has locked up Bacillus anthracis, for example. Does that mean that we can go ahead and openly do research on other aspects of the process?

DR. OSTERHOLM: Well, in a sense it's like the chain of infection. You can break at any one location or minimize one part of it. You basically put the governor on it so that you minimize the situation. You can have a relatively milder agent in the sense of the relationship between disease causation in humans, but a much better way to disseminate it or you can have a really hot agent and a very limited way to disseminate it, and I would argue from the psychological impact I couldn't distinguish them right now in society.

You know, so I think that part of it is that we've got to wrestle with those things. We just don't know, and I think that's part of what we are also dealing with here. I would suggest to you that also -- I mean, let me just give an example. It was referred earlier here in the meeting about the

situation several years ago when a group of researchers de novo created the polio virus from gene sequences and amino acids they bought from their general supply.

Had that same polio virus created an epidemic somewhere in the country because either it accidentally got out or somebody just wanted to now see if it would work, I can guarantee you that had the right connotation of terrorism intent been out there, that would have created a panic that clearly would not have been equivalent to 9/11 post anthrax, but that would have created a major, major issue because it was that psychological impact that, in fact, it was manmade, that it was an agent that we thought we got rid of, and it fits very well with your discussion this morning, Arturo about the idea of once an agent is no longer a problem but it comes back, does that make it even worse?

And so that could have been a very simple situation of just eating some food. You know, just something so simple as that, but it was having that agent available.

So I think there's so many permutations, combinations. I would be fearful for us to come up and say this is the absolute combination, but each one, just as we do when we work up outbreaks in general and Mother Nature made ones, we're always constantly assessing agent, mode of transmission, in susceptible host, and then understanding the psychological impact of what that might be or not be.

And so I think the model is right. I just don't know if we can put an equation in there.

DR. KEIM: So just to maybe restate what you said there, is even though that the entire process of a bioterrorism or bioweapons event would require multiple components, we can't really be sure we know that well enough in order to say that, yeah, it's okay to work on four of the five. We really need to be looking at each one individually.

DR. OSTERHOLM: Well, you know, I would just continue to emphasize that if we have one approach, I would refer us back to the patron saint of hockey, Wayne Gretzky. Don't skate to where the puck is. Skate to where it's going to be.

And I think that what we have to constantly be doing is assuming how to skate to where the puck is going to be, and I think that's what's going to be very hard. If we're dealing with yesterday's problems or yesterday's issues, we will not serve, I think, our country or our world as we need to be. We need to be anticipating these issues. We need to be looking at what the likely problems of tomorrow are going to be.

And with technology changes both informatics-wise, microbiologic-wise, delivery-wise, those problems of today are going to seem, I think, in some cases relatively mild to the potential from an impact standpoint of tomorrow.

Look at the impact that the computer hacker had eight years ago or seven years ago in the computer world, and look at the impact it can have today just because of the way that the Internet has changed the way we do all of our financial business, et cetera.

And so I think we're in the same ball game.

DR. LEMON: Along a related line, I'd like to come back to Arturo's question about when is a microbe a weapon because I wasn't sure I really heard as much importance played to the weaponization of microbes in making that distinction.

For example, is a vegetative anthrax Bacillus a weapon? Well, it might be, but it's certainly not as much of a weapon as an anthrax spore that has been well milled and ground.

And I think this is a very important distinction in terms of the perception of the kind of work that's being done in a number of laboratories. I hear laboratories that work with infectious agents that can be weaponized called bioweapons labs, and yet they're not dealing with bioweapons. They're dealing with microbiological agents that can be weaponized.

Any comments on that, Arturo?

DR. CASADEVALL: I think Stan has is a critical issue that is often, in my mind maybe -- Dr. Franz can comment on this. He has a lot more experience than I do, but it seems to me that if you go and you pull Bacillus anthracis out of the ground,

there is a long, long road for that thing to be in a situation in which you can put in an envelope and cause that kind of harm that we had.

Yet the organism, yeah, it is frozen at that point within the Select Agent list. You look, however at Saccharomyces cerevisiae, and you say, well, you know, that's not a weapon. I eat it, but if somebody could imagine doing something to it in a large amount of spores like that could end up triggering some sort of allergic pulmonary symptoms or something like that and you have weaponized it.

So I think that that is a critical issue that is often not necessarily thought through, that is, that the overwhelming majority of people who work on these agents simply do not have the capacity to make the weapons. Even if they had the intent, the will, and the disease to do that.

DR. FRANZ: I would agree, and I think it underscores a point that Dr. Levy made about the importance of education and awareness. For the public to believe just because you're working with Coxiella burnetti, you're working with a weapon has, I think,

been explained. It's not a weapon at that point.

But education and awareness and not just among scientists, but our leaders and our public and our media and everyone else, and I think that's a very important point that was made earlier.

DR. CASADEVALL: Just to follow that analogy, if you go and you get yourself some potassium nitrite and you get yourself some sulfur and some carbon, you have three compounds. If you mixed them up and you mix them up now in the right proportions, you have gunpowder.

You know, I think a lot of times the analogies that people think, well you have the carbons; you have a weapon; no, it's a long distance from it. You have to some degree with the chemical the weapon potential to make it, but there is a big difference between, you know, working with these things and them being weapons.

MR. NANCE: Dr. Franz, a point of clarification on this issue of intent. If we've got lab personnel already subject to a surety program, the assumption is they're dealing with -- and this gets

back to the issue of what is dual use -- the idea is they're already dealing with something that could constitute a threat, and therefore is, I would assume, dual use by nature. I assume that's correct.

So then the question in my mind becomes that seems like the easy problem. They are already part of a surety program. They're already being monitored, notwithstanding the concern of inside jobs and threats from insiders.

Isn't the threat that we're most concerned with here the sort of asymmetric threat, the small footprint threat that you mentioned in your program? Isn't that a much tougher question in terms of defining or discovering dual use there and what constitutes dual use?

DR. FRANZ: I think in the broader context that's correct, but it's my understanding that the former is more likely to be our mission, within our mission space. It's the research and what goes on both with regard to what might be done intentionally by research scientists in this country, but as we've said, unless there's an international component, that

may not make much difference, but also to help educate and make our scientists aware of potential harm or ill that might come from their research, even if they don't have intent.

So I think the one you're talking about, the asymmetric threat is, as I understand it, less our mission than the other.

MR. NANCE: The idea being that our mission is to insure that the asymmetric threat isn't informed by the good work that we're doing.

DR. FRANZ: That's my understanding.

DR. KEIM: If I don't hear any further comments, I think I will go ahead and adjourn this session, nd we will meet again at 3:20.

(Whereupon, the foregoing matter went off the record at 2:55 p.m. and went back on the record at 3:21 p.m.)

DR. KEIM: All right. We'll call this session to order.

We're very fortunate to have Dr. Anthony Fauci, the Director of the NIH National Institute of Allergy and Infectious Diseases, with us today. Dr.

Fauci, of course, serves as one of the key advisors to the White House, the Department of Health and Human Services on global AIDS issues, and on initiatives to bolster medical and public health preparedness against possible future bioterrorist attacks.

Today Dr. Fauci will provide us with insights into the need for balance between national security, science progress, and the need for individual scientists to become engaged in the process.

Welcome, Dr. Fauci.

DR. FAUCI: Thank you very much, Paul. It's a pleasure to be here.

I first want to apologize to the members and to the audience about my coming at this particular time. As some of you may know, the original schedule had me speaking very early in the process. It was almost as an introductory, but unfortunately I have spent the entire morning and part of the early afternoon at a congressional hearing on pandemic flu, which has its relationship to what we're talking about right now.

So the thought I had as I was taking the Metro here was that it doesn't make any difference what you throw at me. What I've been through this morning, it doesn't make any difference.

(Laughter.)

DR. FAUCI: But I do know, having said that, that what I'm going to say is going to have a little bit of overlap and repetitiveness of what has already had to have been said in the early part of the session. So what I'm going to do is very rapidly go through some of the slide. I'm not going to speak very long, I promise you; to rapidly go through the slides and then just focus on one or two points, again, that I know has probably been addressed, but I just want to underscore it because I really think it's extremely important.

You've already heard the background about the concern that has been mounting about real threats that we are facing, we as a nation and those of us who are in the government working to both detect, plan for, and ultimately develop countermeasures for potential threats of biological, radiological and

chemical warfare.

We are expanding our efforts to develop countermeasures. It's a research endeavor. Some of you may know the history of this, that early on when there was a discussion in the government about where the resources would be put to develop countermeasures, and it became very clear that the best thing to do would be to put it into the hands of the scientific community in a way that by the very nature of the scientific community it is fundamentally a transparent process, but when you say that and you're dealing with, as I'll get to in a moment, an issue of potential dual use, you want to maintain the integrity of the transparency at the same time that you at least are attentive to some of the issues of concern of some of the negative aspects of dual use.

There has been legislation as you are all familiar with, the PATRIOT Act of 2001, the Public Health Security and Bioterrorism Preparedness and Response Act of '02, as well as the Agricultural Bioterrorism Act of '02, which is improving the nation's capacity to respond to bioterrorism and other

public health emergencies.

Now, as I mentioned a moment ago. When you are aware of, as we certainly are very aware of the dual use dilemma, as we call it, there are certain results if not experiments themselves in the development of technologies and information which have naturally raised biosecurity concerns that go beyond the immediate concerns of physical containment, whether you're going to do something in a BSL-3 or BSL-4 and the usual issues that arise when you talk about containment.

You are very familiar, I know, with the Fink report, which tried to address some of the issues of research in an arena of terrorism and how we have to maintain the open scientific discourse at the same time that we, in fact, address the concerns that we have.

Right from the very beginning the discussion of how we can make this analogous to the original recombinant DNA advisory committee because that has a very important history that isn't totally analogous to what we're doing, but analogous enough

that we fashioned the development of the NSABB according to the fundamental principles, one of which in particular I'll mention in a moment.

We go back to the '70s and we see that what these scientists and the regulators in the 1970s had to face is not that much different from what we're looking at right now, and if you look at what the RAC has done, it serves as a public forum for the in depth review and discussion of all of the aspects.

There are internationally accepted guidelines for the oversight of recombinant DNA research, and importantly, it really supplanted what was felt at the time as a burning need on the part of the Congress to formally legislate oversight of these activities, not that that's bad in and of itself, but the potential for interfering with scientific discourse and scientific experimentation was real, and very little of that had to take place because the RAC was originally directed to provide advice, guidance, and leadership, and that's really what we want and hopefully will have the NSABB do.

We got asked early on in a number of

congressional hearings as this was unfolding, the development of the NSABB, is what kind of clout, what kind of enforcement, what kind of security can you be responsible for?

And it took us a while to get the message across that I want to reiterate now that we are not going to be the policemen against the bad guys. We're going to try and set up as we show here a culture of responsibility and framework and guidelines for how different agencies, the Secretary of HHS, the Director of the NIH, and the heads of all of the other relevant agencies, which is why the NSABB and its members, if not ex officio members, really covers the entire waterfront of federal agencies, to provide for them the kind of advice and input so that we can run on what we're calling the culture of responsibility.

And the culture of responsibility is to try and set a framework so that the work that's supported by the federal government, which is the only arena that we can actually have true enforcement capability and enforcement in the sense of if you're getting federal government funds, and you're

deliberately or even without deliberate, but nonetheless do go against certain guidelines that federal funding can be held, but if you look at the agenda, there are a lot of other things that we don't have control over, we, the federal government, and certainly not this committee which is advisory to the federal government. We don't have control over international. We don't have control of people who do not have government funds and doing the research that they do. We can't tell publishers what they can or cannot publish.

So what we really need to do is to just focus in on what is right here on this slide, and that is that culture of responsibility and in that framework to provide the kind of guidance that will allow guidelines to be ultimately accepted by everyone worldwide.

Remember the RAC doesn't have jurisdiction over international issues, and yet if you look at what's happened over the last 30-some odd years with the RAC, it has become just accepted that you would not do something that was not according to the

guidelines that were set down by the RAC.

So in a very indirect way by merely establishing a culture, the RAC has been very effective, and in that regard, what we want and we're getting here with this committee and the discussions today is an active participation of the research community in the deliberations of the NSABB in an open and transparent way, and actually the success of what we do is going to depend on the enormous talent and scientific input that we have into this process.

So I'll stop there. Again, I apologize for coming late, but again, I just wanted to make sure that I underscored that last point of the spirit of what we're doing, and that is that culture of responsibility.

Thank you.

DR. KEIM: Thank you, Dr. Fauci.

With that we'll move into our next session. This next session is going to focus upon a topic that is on the forefront of the minds of many scientists. Specifically the next presenters will discuss various perspectives related to the

communication of dual use research, research results, methods and technologies.

As was true for the previous session, the Board members will have an opportunity to address the speakers during the panel discussion following the talk.

So please, save your questions and comments until that time.

In addition, it's important to reiterate that we will form working groups out of this that will focus upon five different topics, and in particular, this topic, communication, and this will afford anyone wishing to participate the opportunity to deliberate upon these issues in some detail.

So our first speaker is Dr. Judith Reppy, who will talk to us about dual use information issues for the NSABB. Dr. Reppy is a professor in the Department of Science and Technology Studies and Associate Director of the Peace Studies Program of Cornell University, and she will speak about dual use information issues

DR. REPPY: I've prepared a short

statement that is in the briefing books, and I think I should go rather quickly through at least the first few slides because I suspect they overlapped with Dave Franz's presentation to the last panel.

Here I want to emphasize that beyond the simple definition of what dual use is, that security threats today come from non-state actors as well as state actors. So the military users of technology have to be concerned with terrorists as well as with regular armed forces.

Biotechnology is intrinsically dual use. Virtually all military uses have a civilian counterpart, and many, if not all, civilian uses are potentially of interest to the military.

Now, if we're going to talk specifically about dual use information, we know that governments have had for a long time an interest in controlling the spread of both technology and disembodied information. Now, during the Cold War, the Coordinating Committee of Multilateral Export Controls, an international group, CoCom, oversaw a joint list of dual use items that required approval to

be exported to the Warsaw Treaty Organization and other countries of concern.

These controls extended to information. The United States, for instance, if you pass scientific information to a foreigner inside the United States, that's considered a deemed export and has to be technically, at least, the subject of licensing just as if you had exported it by mailing your articles abroad.

The current VASANAR arrangement which followed CoCom after the end of the Cold War is a much weaker regime. It still has these controls, but for a lot of reasons that I won't go into, it's probably not doing the same job.

Now, in biotechnology, if was not included on any of these dual technology control lists, it wasn't a matter of interest during that Cold War period.

The Australia Group, which was founded in 1985, has stepped into this vacuum to extend control to technologies that might be used for chemical or biological weapons, mostly in support of the chemical

weapons convention and the biological weapons toxic convention.

I want to emphasize here again that these control regimes are agreements among states, and they have rather limited use in combating terrorism. They also have just a generic problem that it's very difficult to keep up to date when the technology is changing so rapidly because they're working from fixed lists.

We have a problem, safeguarding biotechnology information, and I've just noted some of the reasons we have that problem. Pathogens are everywhere. Even the small amount can do harm. That's because as you know they can replicated.

Biologists are everywhere, and they also are numerous and diverse, and I think it's important to note that you don't have a tradition in biology as you have in, say, nuclear physics of working between the scientific community and the security community, security establishment. So there's no real existing base, although I suspect one is being constructed right now, but no previous base on which to build

trust in a regulatory regime.

When you come specifically to the question of information, your challenge is great because again, we have this tremendous diversity of journals, over 10,000. You have a well established culture of circulating free prints, conference papers, research proposals, and in general, a culture of sharing information among the scientists.

It's questionable to me at least whether information flows in the life sciences can be controlled in the way, for instance, that nuclear information is being controlled. I'm certain, and I would just state categorically that if it is attempted, the cost will be very high. Whether it will succeed is the thing I think is questionable.

As you know, the Fink Committee considered these issues and had a difficult task because we needed to balance the very strong need to protect the free flow of information because of its importance to biological sciences and biotechnology, with the need to protect some of that information from getting into the wrong hands.

And as Tony Fauci just said, our solution, the committee's solution, was a system of self-regulation modeled on the Asilomar and RAC process, with the local IBCs to review experiments of concern and the journal editors to review journal articles.

Now, this system, I think, has a lot of benefits that relies on existing and trusted institutions at the local level. It gives an important role to scientists. Just the existence of the system should provide a kind of consciousness raising for the life sciences community, and it avoids the imposition of blanket regulations when there are problem experiments, problem papers. They will be dealt with on a case-by-case basis.

But there are a lot of remaining issues, and I want to focus on three of them. I think one question that needs to be better understood is what kinds of information need to be restricted.

It's generally recognized among social scientists at least that tacit knowledge is an important component of scientific knowledge, and particularly the kind of scientific knowledge that

comes out of laboratories.

So in spite of some of the things that you might read in the press, it's not so easy for terrorists to replicate a scientific experiment just because they've read an op-ed piece in The New York Times, let me say.

But you can't rely on tacit knowledge to protect us from that kind of undesirable spread of information, say to the terrorists, because over time tacit knowledge can become codified, and it can sometimes simply be supplanted by something you can buy.

So you can buy kits, you know, from scientific supply businesses that do a lot of the work that used to have to be done by a trained technician. So for that reason you can't just say, well, we know tacit knowledge is important; we're home safe. You have to think about what kind of breathing time the existence of tacit knowledge may provide at least with respect to the most advanced biotechnology research.

As other speakers have said, I would just emphasize that the real problem is the insider

problem, but specifically in this case because it's the insiders that have the tacit knowledge.

A second issue that I think is still outstanding is the scope of the regulatory review. Under the RAC not all industry and government research is covered. Some is covered voluntarily from organizations that don't have NIH funding but only those organizations receiving NIH funding have to follow those procedures.

The question is: is this going to be okay for biosecurity?

I think it's an open question. What kind of controls might we want to extend to those laboratories that are not participating in the current IBCs?

The Fink Committee recommended extending IBC security review to, quote, all relevant research institutions, but I think we walked right away from the idea that we can make a list of those institutions. You guys have to do that.

And finally, I think that there is need to affirm the importance of free exchange of information,

and particularly with respect to two rather tricky problems. One is the sensitive but unclassified category. The government has a policy that fundamental research funded by the government should be unrestricted to the maximum extent possible, and when restriction is necessary, the proper mechanism is classification.

But that policy hasn't stopped federal agencies from trying to insert SBU clauses into research contracts, and I think this is very much an open issue whether that will become a kind of creeping category of information that is closed off from public circulation or whether it will not.

And then there is the issue of classified information. I mean, you might consider the fact that it's not covered is not a problem because the classification, after all, protects it from circulating freely.

But the practice of classification poses its own problems. How to identify information, it must be not too broad or it will cut off important communication in the open literature. If it's too

narrow, it will raise to a very high degree the expertise required to determine what should be classified because each little piece of knowledge has to be inspected.

This is an important issue for the NSABB because any exclusion from the regulatory regime that's being put in place opens loopholes for some kinds of abuse, and particularly use of classification to protect activities from public scrutiny.

So my conclusions are that there's a lot of work for you. There are useful models that have worked in other control regimes, but it's not obvious how useful they will be when extended to the bioterrorism question. It's very important to get the right balance and the costs of either too little regulation or too much control are high on both sides.

And finally, I wanted to emphasize, although I've talked about these problems with respect to the United States, any solution has to be acceptable around the world, and I know you've been hearing that from everybody, and I'm part of that choir. I think that's a very important point.

Thank you.

DR. KEIM: Thank you, Dr. Reppy.

All right. So now we will hear from Dr. Thomas Bowles who will share lessons learned by the nuclear physics and cryptography communities that are particularly relevant for the life science communities.

Dr. Bowles is the Chief Science Officer of Los Alamos National Laboratory and an affiliate professor at the University of Washington.

DR. BOWLES: Thanks very much.

I found this to be a very interesting discussion all day long, and I think you have a very difficult task in front of you.

So I wanted to give you a perspective from someone who has worked in the nuclear physics community and who has also been involved in some of the cryptography issues at the laboratory, how we've dealt with these problems at Los Alamos.

Now, Los Alamos is a multi-purpose national defense laboratory. Our primary mission is maintaining stewardship of the nation's nuclear

stockpile, but we have a growing effort in responding to the threats of weapons of mass destruction, and in particular, we have a very strong bioscience program at Los Alamos which is growing. We have about $60 million of effort a year in it, and it's focused on the intersection of bioscience and national security, and we have a lot of very capable and competent people, in particular, in computational pathomics and in genomics, and in particular, microbial genomics.

So we are a spread of activities at the laboratory. Some of them are purely classified, such as in the nuclear weapons program. Some of the research is very fundamental, and you might almost ask what is this doing in a national defense laboratory, but we found that you really need that breadth of intellectual activities to both stimulate the staff, to provide the core capabilities that drive our national security abilities, and secondly, to prepare for emerging threats because we're not quite sure what that's going to be in the future. And so we need that flexibility.

And I have to say at Los Alamos one of the

hallmarks has been the free and open exchange of unclassified information. We are operated by the University of California, and that sort of academic freedom of expression is something which is at the very core of our ability to excel in carrying out our missions.

So my own background is in nuclear physics. The majority of this research is unclassified. Of course, certain aspects of it do get into dual use, in particular, some of the cross-sections that we measure, which are relevant to issues in nuclear weapons are also directly relevant to nuclear astrophysics issues. After all, the center of a star is about the closest thing that simulates the environment when a nuclear weapon detonates.

And so the mix and match of those two has been a continuing issue in terms of how we deal with the security issues, and more and more we are responding to the needs in the area of homeland defense.

And so some of the technologies that we've developed in my own field of research, which has been

neutrino physics, have carried over now in taking those technologies over into homeland defense by developing new capabilities in low background detection, and this is of particular relevance in trying to detect the entry of illicit nuclear materials into the United States.

In the quantum information area, we have a growing effort in this. This is something which grew out of just the interest of a relatively few staff at Los Alamos in the early 1990s. This was an effort in the group that I was leading in the mid-'90s when I decided that this was something we needed to invest institutional resources in, and so we funded the first demonstration of long distance quantum cryptography efforts.

And this is, again, an area in which dual use is very much relevant. Originally quantum cryptography was envisioned as a means for the intelligence community to provide absolutely secure information transmission, one in which under fundamental quantum mechanical principles you cannot break into the system without being detected. So it's

absolutely physically impossible to corrupt the flow of information in a way which is undetected.

But then, of course, it became immediately obvious that this is of great relevance to people that are trying to protect information of any type. So the people in financial institutions, banking institutions, and so on, who need to transmit information back and forth from different locations across the country in an absolutely secure manner have gotten extremely interested in this.

Quantum computation is an area which is directly allied with this, and again, the issues here range from an entirely new revolution in computer science to the ability to factor large numbers, which is absolutely critical in terms of breaking codes.

So potentially quantum computation provides the possibility of breaking a code in a few minutes, which under our current super computer capabilities would take years to do.

So I wanted to point out some of the issues that are relevant in these different cases. You do have to deal with two types of information.

The first is just purely data information which comes out of experimentation and theory, and the second is those techniques and equipment that have dual use applications and how you approach these is somewhat different.

In both cases, dual use is something which the laboratory has used to advantage, and we're very careful when it goes over from dual use to single use. For example, in nuclear physics it's not the data itself which is restricted, but as soon as you marry the data with the models to simulate the performance of a nuclear weapon system, then it becomes classified information.

In homeland defense, it's not the techniques. It's not the necessary capabilities. It's the specific sensitivities to detection and how we deploy those and our capabilities to detect threats, which is restricted.

And in quantum cryptography, it is the application to specific cases, and many of these deal with specific cases in the intelligence community.

And we take a graded approach to this. So

there are different classification levels that are imposed upon different types of information, and in particular, in the quantum cryptography, a lot of that goes into the SCI, the secret compartmented information, category in which there's only a few hundred people at the laboratory out of our 12,000 employees who have access to that kind of information.

So we are a scientific organization. We publish a very large number of publications. We have about 1,800 open published, peer reviewed journal publications a year coming out of the research as Los Alamos.

And so handling that flow of information has been a real challenge. So we have developed two means of doing that. The first is basically just to exempt certain areas of research from the varying depth peer review in terms of classification, and this is under a mechanism called DUSA, designated unclassified research areas. This is a system in which we propose to the NNSA certain areas which are very well spelled out which we say none of the information in this is of a classified nature. None

of this is essential to national security. That process usually takes about 18 months to get approval. So it's fairly rigorous, but once it's in place, you have a standing exemption, and so things like high energy theoretical physics and so on. Anything in those fields you can just simply publish by saying this falls under this particular DUSA.

Secondly, for things which don't fall into that category they are reviewed and approved for publication by what we call an authorized derivative classifier. It's a person who is very specifically trained in looking at the classified information issues within a publication, and every single thing that comes out of Los Alamos goes through this process.

So my talk went through this process before I came here.

One of the greatest challenges that we have is not so much in publication because there you have got very specific products, you know, which come out and you're dealing with a single item. It's really in mail and E-mail communications, and in the

electronic age E-mail has turned out to be a tremendous susceptibility to security.

So at Los Alamos everyone is trained to recognize what is classified material, what isn't. You are required to renew that training every year, and basically as long as you are absolutely certain that there is no classified information in it, you can hit the send button. If you're the least bit unsure, you go and get somebody to check it, namely, one of the ADCs, and the people who work in the weapons program are required very specifically to attach on the end of each message saying, "This message was checked for classified information."

Now, we do that universally. We don't succeed 100 percent. Our failure rate is about one in ten to the seventh. That's enough to draw tremendous scrutiny from Congress on the laboratory, something in which you cannot entirely succeed without completely closing down the information.

But I'd like to point out some of the issues that arise. There are sort of three areas in which we've had difficulties, one in which content was

sent, which simply should not have been sent. That is extremely rare.

Secondly, the classification level was incorrectly determined.

And third, and this is our biggest problem, is that you will get a sequence of E-mails. So somebody gets an E-mail. They respond to it. they include the original message. It just keeps cascading through, and while any individual part of it may not be classified, when you take two or three different parts of it, suddenly you're in classified territory.

And so the last two we're still struggling to deal with in terms of improving our rejection or controlling the loss of that information, and this is where the culture of awareness is very important because it's basically impossible to provide the detailed guidance required for each and every message that you send out.

Science is continuously evolving. The issues are continuously evolving. The books are never up to date. There's always ambiguities. So people have to use an awareness of what they're sending out

and think about it and say, "If I'm not sure, I'm going to go check."

And there have been many cases in which we have gone to our own local people and they said, "Well, gee, we've never seen this one before." So they go up another level in DOE to NNSA experts and ask for guidance. That's not unusual

And the final one, you know, how do you prevent this concatenation of information? Well, again, awareness is basically the only way you can do this. We looked at the process. It was suggested that we review every single piece of E-mail that goes out of the laboratory every day.

The laboratory generates over 300,000 E-mail messages a day. So our chief financial officer assessed what the impact of doing that was. Our estimated cost was $395 million a year to do that. I think that was clearly an unacceptable solution.

So we've backed off and gone to the sort of cultural awareness, providing guidance, making sure that people are careful.

Then there are issues of communications

within groups and outside of groups. Within groups, you know, we have a mix of people, some of whom are cleared and some of whom are uncleared. We have foreign nationals. In fact, one of the hallmarks of Los Alamos is our foreign national population. We have 540 staff members, permanent staff at the laboratory who are foreign nationals. That is always raised as an issue.

But as long as you have this awareness of what you're discussing, you stop and think, "Wait a minute. Am I getting into an area which I don't want to discuss with this person?"

Generally that's not a problem. You do get into more of an issue in terms of interactions with external groups because those people are generally unclassified, but this hasn't raised any real significant concerns. We do require formal approval of collaborations, and that's not just so much in terms of information control as management wanting to know what's going on and what we're doing.

There is a very specific issue, however, when we deal with people from sensitive countries. So

sensitive countries are defined as those which present particular threats to the United States. There's about 25 on the list of sensitive countries. So countries like North Korea, Iran are typical. Most of these have been put on the list because of concerns about nuclear technologies, but some of it goes beyond that.

One of the questions for the bioscience community is do you want to single out particular countries and the people from those countries as being a particular threat? Are you going to deal with people from those countries in a different manner than you're dealing with people from nonsensitive countries?

By the way, Russia is a nonsensitive country these days.

And finally, for information which you absolutely do have to restrict, you've determined you don't want this getting out into the public domain, you have to provide the infrastructure, which engenders cost in order to provide that communication because you can't just have isolated, for example,

BSL-3 facilities around the country not talking to one another.

So in nuclear physics, generally using dual use technologies has not been an issue. There are a number of cases in which we have to provide special controls for a limited time while we go into certain experiments, and the staff moves back and forth from behind the fence out into the open.

In quantum cryptography, that's more restrictive because a lot of this deals with intelligence information. All of that has to be done inside of a skiff in which the sensitive compartmented information has a specific facility with very stringent access controls where you do the work.

So this automatically limits communication. I don't think this has been a fundamental problem at Los Alamos, but there are issues associated with it.

I think one of the greatest challenges at Los Alamos is this issue with communication with foreign nationals. So all communications that involve foreign nationals requires oversight and security at

Los Alamos. Every time we bring a foreign national in, we have to get approval, whether they're there for an hour or whether or not they're there working permanently.

And this includes a statement of work. Who is going to oversee that work? What access to facilities they're going to have, what access to computer systems they're going to have, and this is reviewed on a case-by-case basis every year to verify that there was no loss of sensitive information or technologies.

And I have to say the restrictions are becoming more and more stringent. We're facing issues now where our foreign nationals may not be allowed access to administrative information, such as how much time, how much vacation they have left, what their savings accounts look like.

And the reason is because all of those are on one computer system at the laboratory that also contains other information that people are concerned about. So do you develop and entirely redundant set of computer systems to deal with that question?

That's very expensive if you decide to do that. We're still struggling with that issue.

And the foreign nationals have felt the impact of this. You know, they have limited access to facilities in information. They have difficulty in doing certain aspects of their job. They feel discriminated against. That is just simply a fact of life that we life with at Los Alamos.

I've tried to convince the DOE that one of our greatest security risk issues facing national security was the restrictions that we put on foreign nationals, not the fact that we have them there; the fact that we don't have enough of them.

You know, in order to address national security issues, we need the best minds in the world dealing with these issues. Not all of those people are Americans. The laboratory was founded by people who were largely foreign nationals back during the Manhattan project.

That statement just received thunderous rejection from the DOE. They don't want foreign nationals anywhere near classified information, even

though in the last 50 years there has never been a documented case of a foreign national accessing classified information.

Every time there has been an issue it has been a U.S. citizen who had access to it. It was the insiders.

So let me finish up with lessons learned. I think the bioscience community is going to have to certainly deal with the increasing rigor that's being focused on national security issues. I think you have a much more challenging problem than we do in the nuclear arena. After all, in the nuclear arena in order to represent a nuclear threat, you have to get your hands on special nuclear material. That generally is very well controlled, and there's a limited amount of it available.

That's not the case in bioscience.

Dual use technology necessarily engenders additional efforts. I don't see any way that this community is going to get away without some sort of process of reviewing all publications and presentations.

Now, you may decide to do that largely by exemption or by exception, but I think you're going to have to have a process which deals with things across the board.

This culture of awareness is absolutely critical, and all of this takes time, money, resources, which is going to be diverted from scientific research because just as the laboratory gets unfunded mandates, you all are going to get unfunded mandates just the same.

Physical access is an issue. You have to decide what you're going to do about that, and in particular, in this community, which is very much an international community, what you're going to do about the question of foreign nationals having access to dual use information and technologies is something which is absolutely critical.

In dealing with this, one of the lessons that we've learned at Los Alamos is that it really would behoove you to form integrated teams between science and compliance personnel to develop solutions for these issues.

At Los Alamos as more and more rigor was put on us over the last ten or 15 years, the response usually was to put the compliance people in charge, have them develop a set of requirements, procedures, and then just throw them over the transom without any thought about what the impact on cost or the impact on productivity was. It was more important to be compliant than to get the work done.

We've stepped back from that and so now everything which comes through the laboratory in terms of new rules and regulations gets checked for cost benefit, gets checked for impact on science, and the best way to do this is to get both sides of the house talking together.

The compliance people have an absolutely valid set of issues that they have to live with. The scientists have an equally valid set. So finding an acceptable overlap of those two is absolutely critical.

And so finally I'd just like to say that, you know, we have dealt with these questions at Los Alamos and at the National Defense Laboratories for

more than 50 years, and I would just like to offer the services of the laboratory in any way that you might find useful in helping you to deal with these questions.

Thank you.

DR. KEIM: Thanks, Tom.

So next I'm pleased to welcome Dr. Phil Campbell, who is the editor-in-chief of Nature and a Director of the Nature Publishing Group, to share with us some of his perspectives as a member of the scientific publishing community.

Dr. Campbell.

DR. CAMPBELL: Thank you very much for the invitation to speak at this meeting.

The title as in this green paper says that I'm giving the perspective of scientific journal editors and authors. We reject 95 percent of our authors. So I'm sure they wouldn't like the idea that I was trying to represent their viewpoint.

And just to say a little bit that's somewhat more serious about the journals, I'm certainly only giving my viewpoint. The journals such

as Science Magazine, Cell, PNAS, and Nature, we are all in competition with each other, and sometimes that becomes an issue, but on this issue I would say there's been a lot of collegiality and discussion and I'll give an example of that.

So my purpose here is briefly to review to some history and also provide an overview of some of the key issues as I see them.

So there was this meeting that has been referred to, and I just put that up as a point of reference. Those were the people at that meeting in January 2003. Following a National Academy's meeting, this was a meeting convened to get editors together to discuss the issues many of which are being discussed by you.

And I would say that there was a large degree of consensus during that discussion about the minimum amount of regulation that we could all accept, and also at that meeting were not only the editors and some of the authors of some of the more controversial papers that have been published up to that time, but also representatives of government departments, as you

can see on this slide.

And I would say that they were there to help us regulate ourselves to adopt a culture of responsibility, to use a phrase that's been used at this meeting. You were very aware that Congress were concerned about some of the publications that have recently appeared, and we were therefore concerned to, as was again being said at this meeting, to try and anticipate and, if possible, preempt any overreaching regulation.

We came out with a big statement which you can find in the journals from that time. I just wanted to highlight one that actually took a bit of soul searching before we were willing to put our names to it, I think, but nevertheless we did make the statement that there were circumstances where just for security reasons we might not publish the paper.

And there was some controversy following that announcement. There was a letter in Science saying that there needs to be a lot of clarification about just what it is that you might regulate and prevent ourselves from publishing voluntarily, and

that issue is absolutely with this Advisory Board.

There was a strong statement made on their own Website by the Public Library of Science, which as many of you know, is a recently formed publishing group set up to promulgate open access publishing, that is publishing that is paid for by the author rather than by subscribers. So it's completely available free of charge on the Internet.

They took a very strong line that any such control was akin to censorship.

And then if you look around, you can find people who have concerns about openness, and I just mention two people here, and I won't go into what they say, but they are some of the people who if you wanted to get the most skeptical point of view about just what journal should be free to publish, they would be a good place to start.

So we did what we had undertaken to do. We established an informal group of advisors with defense connections, including in Britain Porton Down people, in the U.S. some of the people at the national labs. We held informal discussions with people about

how this should work best.

We set up an internal framework for consultation, and we published the policy, and the policy is very straightforward. We maintain a network of advisors specifically for biosecurity issues, and whenever there is a paper that comes in where an editor's box or a potential problem, that is shared with me, with the Chief Editor of the journal concerned, and with a couple of other people within the editorial group.

So just to remind you if you're not familiar, we have Nature itself as part of this group, but we also have a number of related spin-off journals, such as Nature Immunology, Nature Genetics, Nature Cell Biology, Nature Medicine, Nature Biotechnology. So all of those journals share information where you get into this sensitive situation.

And then once a decision has been reached, authors will be informed if the biosecurity advisor has informed that decision.

So, so far, so good. Having talked about

that policy in various places, a number of questions do get asked, and I can't say that I'm necessarily satisfied with the answers I give.

So one question that was asked of me was why keep the security advisors' identity and advice confidential. I mean, it's even arguable that referees on the technical side of the paper shouldn't be anonymous. But we stick to that as a policy, and in fact, the practical reason why we keep the biosecurity people anonymous is also for two reasons.

First, it would be a cultural leap for us to announce those identities.

And, secondly, actually a lot of the time they are also giving us technical advice.

But nevertheless, we did get some feedback from one of the papers we published, which I'll mention later saying that actually this policy needs to be more transparent and more openly regulated or maintained, rather.

What happens with a paper that's rejected on security grounds? This is a definite issue, I think for this Board to think about. Currently the

default is author confidentiality overrides all other needs. There is no system in place; there is no agreement in place by which if we reject a troublesome paper purely for security reasons we will then do anything to prevent it being considered by any other journal. Obviously within our group we would communicate that information.

But for the moment there is no formal procedure by which we set up, we agree to share that sort of information.

Of course we can exert our discretion. So that applies not only to this. It would apply to an episode of misconduct or professional misconduct, for example. So we do try to act responsibly if the need arises.

Is this agreement that we've all reached or this consensus perhaps is a better word, of how we would act to those journals that I've identified before, is that international? Does it include foreign language journals, for example?

The answer is no. It is not very international. There are a couple of publishers from

outside the U.S. represented amongst all of those journals, but it has not been spread as a consensus statement, if you like.

And what actual questions do we ask the security reviews? And on the whole we have been understanding that the papers we would send out are not obvious weaponization papers where you can point to the recipes that I'll mention in a minute and that you've already had highlighted from the Fink Committee, for example.

Given that we don't usually handle those sorts of papers, it's not so obvious to try and come up with a menu of things for these referees to look out for. So on the whole, we've been pretty open ended and simply asked them the general question.

So what has happened in practice? Before giving this talk, I checked with Don Kennedy at Science and Sam Kaplan at the ASM, and Nick Cozerelli at PNAS. So the Nature journals, we've sent out several papers during the year since that agreement was reached, but no decision has been affected by a biosecurity consideration, but no papers have to be

modified or delayed or in any way affected.

Similarly, the same applies to Science magazine.

These figures are imprecise and, in fact, you heard better figures and more authoritative figures early on in the day, but as far as I understand it, none of the American Society of Microbiology papers submitted to those journals have been rejected for purely security reasons.

I also included a statistic that somebody gave me, which is very similar to what we have as well that most papers now are co-authored by about five people, on average. Sometimes you have a huge number of people. Sometimes it's only one, but on average five or six people seems to be an average, and in the ASM's case, 60 percent of those collaborations include multinational partnerships.

And then PNAS until very recently was in a similar situation. I'll come on to the recent exception.

So there seems to be a general consensus that is emerging through the years since we had that

discussion that open publication is a key to public health. The details of pathogenic mechanisms used by organisms to outwit the immune system are necessary to develop new treatments. Some experiments with hybrid pathogens against scourges that currently kill many worldwide are worth the risk.

Properly contained experiments in appropriate facilities are crucial, and public outreach and education are crucial to avoid misunderstandings and inappropriate regulations.

So one or two general statements which go over a lot of what has been said, and in fact I'll skip most of this because it has all been said, but certainly the SARS genome demonstrates the fact that you can have immediate health benefits by publishing some of this stuff.

You get the benefit of economic health and academic quality and you get openness attracting talent and you get openness encouraging international collaboration.

You also get a sense of consensus internationally. That's one of the virtues of the

internationalism of science. So you can get international activities leading to a consensus in what constitutes appropriate action as we seem to have seen with the RAC. Overly tough regulation of publication, in one country will be ineffective and classifying certain research unilaterally would also create incentives for scientists to move research programs elsewhere, and of course we've seen that with stem cells moving from the U.S. to other countries.

I think there is a key issue of trust, and it has been referred to already. The perception of the U.S. in particular at this time, there is no question that editors outside the U.S. and scientists will be wary about U.S. motivations. The visa situation, which we're all familiar with, certainly led to a chilling of the climate.

And we were all aware that some of the key information resources that everybody depends on generally bestowed on us by public funding in the U.S., the National Library of Medicine's PubMed is a key example of that, are ultimately under some sort of government control and so there is a concern as to

what might happen if people get concerned about some of the papers appearing on that.

So another question that came up at this meeting we had and are still waiting for a really good answer, is this "it." What are the "its" that would stop us from publishing these papers?

And I will refer her to a paper in the Journal of Homeland Security, which is a free access on-line journal. You can all find it, which seems to me to anticipate not only this particular set of issues, but also some of the others which I'll come back to, by Ray Zilinskas and Jonathan Tucker, who work with the Monterey Institute for International Studies, and in fact, Jonathan Tucker is here because I've met him.

And these are just a set of six types of work about which one needs to have concern, and I certainly won't talk through them. I think you look carefully you will see some differences between those and the Fink Committee, for example which I'll refer to later.

So I just put this on the agenda as

another source of information as to what we might think about.

I also wanted to highlight some points made by George Post, who many people will know at the National Academy meeting itself back in 2003, which talked about not only the obvious weaponry that we all discussed today, but also highlighted other areas of research which we need to be aware of in the future.

So we have deliberate engineering of immune escape and stealth viral vectors, the over production of host inflammatory mediators that produce toxic shock, the knocking out of genes that regulate key cell processes, such as cell proliferation, small molecules that disrupt molecular circuits, networks in immune response, blood clotting systems, and so on, and also more mechanical disruption.

And a lot of these areas are the most exciting end of research. So there is definitely dual use in other areas than microbiology, for example.

So we also had the Fink recommendations which you've seen before. So I won't go into that.

So since that meeting we have published

and other journals have published papers which were in many cases totally uncontentious. They were shown to security experts as part of their assessment, and I just wanted to highlight those as examples of the sorts of papers that are coming out all the time.

And I can't resist mentioning quite by chance that the person I chose to quote making clear the virtues of the publication of the anthrax genome is a member of this committee, and I couldn't have known that until yesterday. In fact, I got the slide together some time ago. So there you go. That made it clear that publishing that genome actually had a definite benefit.

We did get some feedback from another paper that we published on identifying the cause of virulence in the flu in mice from the 1918 strain proteins.

And I won't go into this. The point of this slide is simply to say what they did and highlight that there was a genuine scientific insight in what was going on. The bottom line of the paper was that it showed the role of hemagglutinin, in

particular, in the pathogenicity.

We got concern coming back after that, which was in relation to the safety of the labs, a concern as to why do the work at all, and a concern over the lack of transparency and demographic accountability.

I'm not going to go into those issues. I'm perfectly confident that we were right to publish that paper.

Then we come to something that has been referred to, and it's in the news at the moment, this paper that was submitted to the National Academy of Sciences, the proceedings of that institution and concerns the introduction, a theoretical mathematical study about the impacts of the introduction of botulinum toxin into the milk supply in the United States.

And just to very quickly discuss what the paper does, it says "in press." In fact, it's now published on line.

The input was to take various scenarios of toxin introduction, nothing new or hard to discover

for those people who want to find that information, and produces an output in the range of impacts on health and mortality and analysis of responses to protective measures highlighting security needs.

But then there is a course of events that I think is worth summarizing because it gives rise to issues which I will quickly summarize in turn.

The author checked with HHS. HHS advised against, but the author denies that he got that response from the HHS. I'll come back to that.

PNAS followed all of the procedures that they said they would follow. The referees all approved publication of the paper. As is standard practice with the NAS, they press released this paper among others that they were going to publish and issued it in embargo form to journalists.

A journalist contacted the HHS and asked for their reaction to the idea that this paper was going to be published, and the HHS then contacted the National Academy of Sciences to express the same concern that they originally expressed apparently to the author.

And the National Academy decided to delay the paper's publication and had a discussion meeting and then proceeded to publish it.

And you can find a full description of that order of events in an editorial by Bruce Alberts, the President of the National Academy of Sciences.

But he raises some issues, it seems to me. So one is that there is an issue of responsibilities to researchers and the HHS and other agencies to pursue an alert like that in a way that is fairly rigorous and robust because we have in this particular case a difference of description of actually what happened and who did or did not get back to who.

And that in itself is unfortunate, but the question is: what is there in place anyway for researchers who are acting responsibly on their own initiative once they have done a piece of work that they consider to be sensitive?

So I would say it's a straightforward issue for this committee to address whether or not a system like that could be set up and what that alert system should consist of.

There is a question which is whether the paper should have been submitted to a high profile journal, which the PNAS is, and whether that journal should have accepted it. I'm not going to try to act in Nick Cozerelli's place and make a judgment on that particular last point because I haven't seen the referee's comments.

Nevertheless, I do think that is an issue, whether that sort of paper is appropriate for that particular journal.

Then there is a question what is sensitive research anyway. How should government respond generally? What is the appropriate code for researchers for communicating dual use results?

There is a lack of guidance out there, and I think from what I heard about the conversation that took place between the government representatives and the NAS, there was a real risk that an overreaching negativity about the very idea of publishing any such paper could have, as I say, be over reaching, and without better guidelines, it seems to me, such discussions are undermined.

So there I think this particular Board has a very key role to play.

I won't go through the details here of papers that we have also published in another area of interest to this Board, which is synthetic biology. This is an example of synthetic genomics that we published. There was another paper that came out very soon after that in nucleic acids research.

And the key point about these papers is simply to make the point that it is (a) important, (b) rapidly turning out to be a fairly cheap sort of technology that would be widely available.

But I did want to draw a little bit on synthetic biology itself and some of the issues that it raises for journals and for the community. So here's a description, and I won't go through all of this, but it's a visionary description from one of the pioneers of the discipline, Drew Endy at MIT. This is an article written by a first rate journalist, Oliver Morton, in Wired Magazine, which you can find freely on line, January 2005.

And basically it's describing a program by

which one can assemble a set of parts and proceed to make artificial chromosomes, artificial replicating organisms which don't necessarily follow the geometry, as it were, of naturally evolved organisms.

It's engineering as well as science. It's precision design rather than what a lot of people would call DNA bashing, knocking out genes and seeing what happens. It focuses on the artificial production of cell components. It's a methods sort of activity. So there are methods journals out there who have different criteria from scientific journals in the sense that there isn't necessarily any insight coming out of this work. It is more like a technology.

The cost productions issue I've mentioned. So you get into questions of should there be registration of the equipment that these people are using. Is there a need for engagement with security communities and stakeholders, to which the answer seems to be yes.

Is an Asilomar-type moratorium, which has been suggested from time to time, practical? It seems to me that the answer is definitely not. In relation

to codes of conduct we're saying because this is essentially an engineering community and still a very small community, they recognize that they themselves can moderate or think about their behavior in the context of the issues that this Board will deal with. Because engineers, like medics are more akin, more used to the idea of codes of conduct, and those codes of conduct which have bite and which can actually lose you your license to practice.

So although this is being founded in institutions which don't have that strong tradition, nevertheless they themselves recognize that this is something that may be necessary.

I think the final point is also important. It's not materials that come out of this work that is spreading around the world. It is information that you can easily post on databases.

I think compliance frameworks are one of the last things I want to talk about. You have in universities well established frameworks for compliance for safety regulations and research involving humans and animals. I think these are less

well established for other codes of practice. So I think that is an issue.

The same applied to journals. We have well established codes of conduct where research is done for the journals themselves insisting on the sharing of materials and conditions that we have to publish about whether guidelines have been followed on ethical issues to deal with the research on humans.

But we have far less systematic guidelines for ethical boundaries and in cases of misconduct.

We have no inter-journal framework, as I mentioned before for biosecurity concerns.

Finally we come onto the possible restriction processes that one might want to do, and here I'm just going to flick very quickly through several publications that have appeared or presentations that have happened recently.

There's this paper I've already referred to. There is the paper that has just come out in the CBW convention's bulletin by Elisa Harris and John Sensenbrenner, and this is a framework that is worth just thinking about because it does go up to the

international level, where you have WHO type frameworks at the top and then you have a RAC type framework beneath that at the national level and then you have IRBs and other local arrangements.

There was an exercise that I won't go into. I'm sorry time has gone on, but I won't go into it here, but this again was an exercise done at the University of Maryland where they actually got together a group of people, five scientists proposing biodefense studies and 20 peer reviews to look at those proposals and to see what sort of consensus might emerge in judging the risk.

And it seemed to the organizers of that meeting at least that you could get some sort of consensus and there was some clear criteria that emerged.

So this Board may want to think of organizing some such exercise again.

But there are these problems on restrictions, and I think almost all of these have been mentioned already, except as far as journals are concerned, although Nature and Science and other

journals of that ilk have got quite a lot of resources behind them, most journals do not have a lot of resources behind them, and therefore, issues of compliance, issues of process that you may want to impose on them or recommend to them, it's not obvious that they're always going to be able to do them if they take any resources to get underway.

So I just want to end on what I call E-truisms, which is that journal editors must show responsibility, and I hope I'm showing that in some ways we already are, but we are absolutely open to further discussion about what else we must do.

As has been said here already, scientists must show responsibilities themselves, and I also want to include my favorite quote which came out of congressional testimony, which just highlights the value of openness. The traditions and structure of research in the U.S. today depend on replication and reputation, which means that sufficient data and methods to allow that must be published in peer reviewed journals. Such publication also mitigates fraudulent results, sloppy science, and political

biases guiding important policy decisions.

Recent well publicized incidents of scientific misconduct underscore the merits of this system.

Thanks.

DR. KEIM: Thank you, Phil.

So we'll go ahead and move on to our next speaker. As is obviously from many of the talks today, the issues surrounding dual use research transcend our national borders. We will now hear from Ms. Wendy White who is the Director of the Board on International Scientific Organizations at the National Academy of Sciences.

She'll give an overview of international discussions concerning dual use research.

MS. WHITE: Thank you very much.

It's a pleasure to be here and see you all still here. One of the advantages of going last is I get to now be highly selective on which slides I show you and which ones I think you've already seen.

There's been some discussion already this afternoon about the need to internationalize this

debate, and I have been asked to concentrate on that issue. So I'm going to tell you a little bit about an international forum on biosecurity that recently took place in Como, Italy, March 2005.

This meeting was co-sponsored by the International Counsel for Science, the InterAcademy Panel, which is a network of about 100 Academies of Sciences from around the world, the InterAcademy Medical Panel, and the National Academy of Sciences.

We had scientists from more than 20 countries at this meeting from both the north and south. I think the first people who signed up were from Mongolia, but we also had participants from Zimbabwe, Brazil, South Africa, China, and so forth.

The forum divided itself into three working groups, one to discuss guidelines for principles of professional conduct. The other was dissemination and communication of research, which was the one I was in and will focus on, and codes of conduct.

And I'll point out that there are many people in this audience who were at this meeting, and

I would invite them in the question and answer session to add anything they want from their working groups.

The forum was a direct response to the Fink Committee report, and its agenda reflected the growing awareness that there are rapid developments in life sciences and biomedical research. Much of this debate we've already seen today.

What we intended to do in this forum was broaden the debate and advance the awareness of these issues in the international community, and to some it served as a major convening and coordinating mechanism. All of the people there were sharing information about what was happening in their countries and what they were doing to address these concerns.

A number of the participants at the Como Forum also then participated or will participate as invited experts at the state's parties to the BWC convention.

The overall meeting outcome is very simple. It was the first time many had seriously considered the implications of dual use, but all were

convinced at the end of the meeting that they as individuals and the scientific community as a whole have a major and pressing responsibility in this area.

The working group that I participated in was specifically on dissemination and communication of research, and our group started by looking at this principle of the universality of science, and a lot of this principle has been discussed in part today or in different parts, and I put it here on one slide. This is what the principle states and this is what scientists are talking about when they say or are referring to the universality principle.

It's the freedom and the conduct of science, and it covers three critical areas: the freedom to pursue science and publish the results; the freedom to communicate among scientists and to disseminate scientific information; and the freedom of movement of scientific materials.

This principle has been stated by the International Council for Science, ICSU, which was one of the sponsors of our meeting.

The principle goes on to affirm the right

and freedom of scientists to associate an international scientific activity without regard to such factors as citizenship, religion, creed, political stance, ethnic origin, race, color, language, age, sex, and my committee always adds gender, saying sex and gender are two different things.

The universality of science many feel has been somewhat challenged in the last number of years, but because the intrinsic nature of science is universal, its success does depend on cooperation, interaction and exchange that often goes beyond national boundaries.

For this reason scientists must have open access to each other and to scientific data and information. The changing political climate and concerns about international terrorism have challenged this principle. Threatened boycotts on scientists from other counties, restrictions on publications and exchange of materials, withholding of travel visas, something with which I'm very familiar, and work permits are just a few examples of these challenges.

And the restrictions can have a negative impact on the overall value of science, both nationally and internationally.

The second issue that my working group focused on was the changing nature of scientific publishing. You've heard a lot about this already today, but researchers face increasing pressures to publish faster and in more internationally accessible media. They work in environments dominated by Web based publishing.

I read this morning that by the year 2020, 90 percent of newly published work will be in electronic form. This is something that the British library says, and only about 50 percent of that will actually be available in print as well as electronic.

There are more than 315,000 biomedical articles published each year, and our group also discussed the vast growth of international science. The number of authors from more than one country has increased 200 percent since 1981. International collaboration accounts for more than one-third of all co-authored articles. That figure is probably low,

but that's across all of science, not just in biomedical science.

This means that there's almost a guarantee that every biomedical article written will be published somewhere some time by someone. Controlling this environment then is extremely difficult, if not impossible.

It's not enough to focus on the U.S. environment, and I would refer some of you to I think what would be a very interesting case study on Kemron, which was the cure for AIDS that was announced by the Kenyan Medical Research Institute in 1990. I think there are some very interesting parallels there.

But the focus on traditional publishing outlets is also not enough. Information is widely and instantly available on the Internet, preprint servers, textbooks, Web pages, institutional repositories, blogs, theses, and many other non-peer reviewed publications.

We did focus quite a bit on the international perspective. I will not read this quote, but our participant from Zimbabwe started with

this, and I think it's rather interesting, where he sees what the real challenge is is that if we try to control information too much, then his country would have a hard time doing the research it needs to tackle AIDS and HIV.

We also had one participant, who consulted with her South American colleagues after the meeting, and she asked them to what extent they were aware of these problems, and she found that to a large extent most of the people she talked to were not even aware of the dual use issue.

She also cited a lack of adequate legal national frameworks to control dual use, biological agents, and related research. She pointed out, too, that the rigor in science is somewhat less in some of these countries. There are fewer peer reviewed publications and less of an awareness of the responsibility needed by scientists.

She suggested to us that we encourage international programs that raise the awareness of scientists around the world of these issues, that increase their capacity to deal with these issues,

that help them identify experts who might come and help, help them address concerns of policy makers and officials, and help build networks to disseminate the kind of information that is needed.

So we'll move on to the Como Working Group conclusion, and to a large extent our working group conclusions echoed the findings of the January 2003 meeting at the NAS which Dr. Campbell has just thoroughly described.

We made a distinction between fundamental and applied research.

And in the end, all of the researchers in our group recognized that sensitive information does exist, that efforts to control the dissemination of such information at the end of the research chain, that is, at the publication stage, are neither desirable nor practical.

Once something is peer reviewed and published or on line, then it is far too late to control.

Our working group also found that the benefits of increasing access to information and

openness in science are enormous, and the scientific process works only in an open environment in which research results are shared and built upon. You've heard that over and over today.

There was a quote in the Washington Post from Sunday, and I think it sort of summarizes what our working group thought. The best defense against those who would use it, and she was referring to information, as a weapon is to insure that our own scientists have better information. This means encouraging publication.

However, researchers must address public confidence issues and government concerns by taking responsibility for the knowledge they generate. Our group concluded that the shared ownership of knowledge is often a better safeguard than restricted access, but also we agreed that researchers could do a far better job of communicating with the public and with policy makers in persuading both communities of the importance of the universality of science.

And that's how you find me if you want.

Thank you very much.

DR. KEIM: Thank you, Wendy.

So at this point we move into the discussion with the Board and ex officio members. I would like to thank the speakers and also ask you to return to the podium, please.

While they're returning, I'd like to remind the Board members and the ex officio members to use your microphones. Evidently sometimes during the previous discussion when individuals would turn their mouths away from the microphones people in the back of the room weren't able to hear us. So let's try to make sure that we use the microphones effectively.

With that I would open up the floor to any discussion. Harvey.

DR. RUBIN: I would like to ask about the activities at Los Alamos. It seems to me that's a relatively unique operation, and many of us come from universities where we don't have that kind of infrastructure that you have at Los Alamos.

Do you have any thoughts on the same sets of control that universities would be able to employ given the difference in the nature of the research?

DR. BOWLES: It's certainly a challenge because the laboratory has invested significantly in the resources, the infrastructure to do that, but I would say the thing which is common across all of these things is that any system that you put in place is going to fail if the people who are involved in it have not bought into it, who are not aware, who are not going to participate in it.

And a lot of these issues, our first line of defense, you know, against unintentional release of information is the staff itself. And I think at the national laboratories there has been this issue which spans, you know, the entire spectrum of activities where people are inculcated with the need to think about what you're doing, to be careful, to be aware, to be accountable, and you don't normally find that to the same extent at the university.

So I think a lot of this is going to be an education process in getting the faculty and the students at the universities to be aware that this is an issue. It affects them; it affects the people around them. And they need to participate in this.

DR. RUBIN: Given that there isn't the infrastructure at the universities, I mean, from your perspective in the physics community and the computing community, have there been things that have been published from universities that you would consider are major risks and threats to security?

DR. BOWLES: Not specifically. What does happen is that we have seen cases in which there is a low level of concern in which people have just on their own put together information which any one part of it by itself is unclassified or nonsensitive, but when you put it together, it actually is sensitive.

And one of the dilemmas we found ourselves in, in those cases, is how do you communicate that because it's a security violation to tell somebody that that's classified. So, you know, it's the old Catch-22.

DR. RUBIN: So if you continue the line of logic then, in the vast history, much longer in your field perhaps than ours, if there has not been a publication that's resulted in something that would be considered to be a security leak, maybe we don't need

this big infrastructure at all.

DR. BOWLES: That's a very good question. The aspect of it which I think you are going to have to deal with in particular is the international aspect in terms of countries in which we know there are organizations which may want to threaten the United States and in which the governments are not acting in a responsible way to quell those groups.

So do you somehow single out certain areas and try to restrict their participation and efforts? And this cannot be a unilateral approach. If the United States decides, well, we're just not going to let anybody from Country X come in and have access to any of this technology or any of this information; we're not going to allow students from these countries to enroll in the universities here, the only way that that will be effective is if the entire international community buys into that.

How you deal with that issue is very, very difficult.

It is very different in the nuclear arena because here we're dealing with a limited set of

countries which have nuclear capabilities and a limited set of technologies which are very specifically a threat to international peace.

The problems that you face in bioscience are much more ubiquitous and so I don't think necessarily the same solutions that we've employed in the nuclear arena are going to be effective in the biothreat arena.

DR. SORENSEN: As a university administrator, I'd like to suggest that the mentality that dominates in many quarters in research universities is that faculty members are semi-autonomous agents, some of whom report directly to God and some report to deans and department chairs and ultimately the president of the university.

So to try to imagine a president, just to take a random example, suggesting that we structure apparatuses, that would be analogous to those in federal laboratories is difficult to imagine.

I envy you the ability to have that kind of coherence about the things that are important and the things that are less important.

DR. BOWLES: Let ms just respond to that. You obviously have not been to Los Alamos.

DR. SORENSEN: I wasn't going to make any derogatory comments about recent problems.

DR. BOWLES: No, but part of the issue about problems and so on is what culture do you have, and one of the great strengths of Los Alamos has been the individuality and open academic freedom that our staff have enjoyed. And there is continuing pressure to clamp down on that, and the laboratory is trying to find a balance between maintaining the creativity, maintaining the best intellectual atmosphere to retain our best staff so that we can address these issues, at the same time as we are being compliant.

And I sit on the Council on Research at the University of California, which is the chancellors of research and their counterparts at the three UC labs, and the universities are being forced to address some of these issues.

For example, dual use export conditions. That has been a major topic for discussion at the council on research because you by law are compelled

to make sure that you are not transferring sensitive technologies to foreign nationals without due controls.

So there has been a lot of resistance at the UC campuses about what that means and how you implement it, and that was why my last point is very important. You need to work with the controllers, with the compliance people to figure out how you're going to implement some of these conditions.

This committee, the NSABB, is going to come up with a set of suggestions, recommendations, policies that will address some of these issues. However, how those are implemented and how they affect your institutions back home is a separate question.

And if in your deliberations you take that into account, you will be much more effective in being able to translate what your decisions are here and how it impacts people in daily life.

DR. SORENSEN: And I want to make clear that I salute you for the courageousness of the comments that you made. I salute you for your efforts in that respect. It's just that sometimes trying to

organize scientists around common themes and common code of conduct is like herding cats. It's very difficult. That kind of autonomy is valued in the culture of research universities.

DR. RELMAN: I think the presentations in this last session are extremely interesting in their juxtaposition and almost in the kind of culture differences there are between some kinds of science and others, and in particular, the kinds of nuclear physics science that Dr. Bowles presents, and the nature of the biological sciences today and into the future.

I'm struck by how different and maybe in many ways almost nonapplicable some of the practices and rules and kinds of procedures are that were first described in the realm of nuclear physics and then finally by the very different view of the future that Wendy White presented in which it seems almost inevitable that biological information in its diversity in ubiquity and its easy of digitalization will become widely disseminated in electronic format in a Web based manner.

You can almost see ten years from now that biology will be distributed as bits, bits not only in terms of procedures and steps and methods and insights and so forth, but literally digitized information about biological agents, i.e., as in the ways of synthetic biology.

So I guess that leads me to wonder whether we can think about ways in which the biological community can self-organize in a Web-like manner to see where bits can come together that have potentially greater levels of potential harm and untoward effect than the realm of all biological information on the Web do otherwise.

In other words, is there something special about stories like publications that will still exist in the future that we can still monitor somehow in electronic format as perhaps journals become less relevant but still packaged stories maintain their relevance in biology?

DR. CASADEVALL: Following up on that, I'm also struck by the -- I think the nuclear experience is very important for us to consider as something that

has been implemented and exists, but then you step back and you look at the differences and the differences are so huge.

On one hand, nuclear weapons are human made. Biological weapons exist. That is already an enormous difference. One of them requires an infrastructure, an industrial infrastructure. It requires materials. It requires a lot of things.

The other one requires essentially very little, and as Dr. Relman was pointing out, these agents already exist in nature, and in fact, the greater threats, I think, that we face are the continued emergence of these organisms as a threat to humanity.

DR. BOWLES: Let me make a comment in response to both of those. I think you are absolutely right that there are very significant differences in how you approach the nuclear threat and how you approach the biothreat, but one thing that it has in common in terms of openness of information, after World War II, there was a discussion about how do we restrict the information to make sure nobody else ever

gets this information.

And the statement back from the science leaders, the ones who developed nuclear weapons during World War II was you can't do that. It's impossible. There are physical laws which people will go out. They will study. They will explore them. They will figure out how to do this.

The only way that you can respond to this is to stay ahead of the curve. So that our capabilities in terms of response and so on exceed those of any of our adversaries.

So I agree with that statement, but the problem is that hasn't prevented the legislators from imposing dramatic restrictions on how we try to protect that information, and I think that's one of the issues this Board is going to have to deal with.

There's going to be tremendous pressure from agencies, from Congress, from the public, to put controls on this that will protect them, and how you do that and how you respond to that pressure is going to be extremely important.

MR. NANCE: Dr. Bowles has already pointed

out there is already a compliance regime in place under the international traffic and arms regulations and the Export Administration rules dealing with biological materials and dual use materials that may have a military application , and it's a pretty broad definition of what falls under those rules and what requires a license or a commodity jurisdiction request, which is a program that's administered by the Department of Commerce, Department of State, and Department of Defense jointly.

I know there's a lot of research going on within this room and certainly at this table related to what might be considered dual use technologies under ITAR, EAR.

I was curious whether any of the members of the Board have run up against that in terms of chilling their ability to do research or restrictions on foreign nationals and their labs. Nobody?

DR. LEMON: I think it's fair to say it's a major and growing concern, particularly when you realize that if you ship something within the United States to another university and it's received by a

foreign national at that university, that's a deemed export, as was mentioned by one of the previous speakers. I think a lot of people may not be aware of that.

MR. NANCE: Well, just having the foreign national working in the lab itself is a deemed export, right? I'm surprised that the comment had not come up prior to this because this is already a restriction that exists on labs today.

DR. FAUCI: It goes beyond foreign nationals that are identified from countries that are countries of interest; however you want to classify them. Just the whole issue of having post docs go back home and get back into the country is sometimes chilling right now. I mean it's a totally different atmosphere of the flow of foreign postdocs who come in and out of the country who are out and trying to get in or are here and go home and have to then go through their own embassy to get back.

That is an issue that I think is very pervasive in academia.

DR. LEMON: I would say, Tony, if we're

trying to establish a global culture of responsibility, insuring that that flow continues unimpeded is very important.

DR. FAUCI: I agree with you completely, and that's one of the first easy steps to do. When there's obviously not an issue with a person, they get caught up in the bureaucracy that has evolved. It's too big a blanket of bureaucracy as opposed to specifically looking at areas that are really sensitive areas.

So there are a lot of people who get caught in that net making it, I think, from a morale standpoint, having less enthusiasm about coming here to study.

DR. ENQUIST: I'd like to make just a couple of comments about types of journals and journal publication. Maybe Phil Campbell could expand on this a little bit.

Journals like Science and Nature are very high end journals, and as you said, publish about five percent of the papers that are submitted, but a lot of other journals, for example, the society journals, the

SM journals for example, are journals of record or in my case Journal of Virology for progress in virology.

We publish a lot more papers that essentially document the progress that's going on in virology.

The second thing is that this type of publication is also very important because it documents the work that's being done by individuals for job security, for promotions, for tenure and whatever. So there's a whole aspect of the scientific enterprise that's involved in publications of this type that you don't want to mess with without thinking carefully through this.

The second thing is that many journals, the ASM journals in particular, have a set of requirements for authors that, again, lead to the way that we do science. For example if you publish in an ASM journal, you are required to make all of the reagents that you have published available to anybody who asks so that the work can be repeated.

I must say that one of the jobs that I run into that's distasteful is trying to force people to

do this when they decide that they don't want to do it because of competition or whatever.

Basically, again, the whole idea of publication has some implications to how science gets done, and it's very key to me that the enterprise's fragility really lies on this whole layered effect of what publication really means to the way that the enterprise works.

DR. CAMPBELL: I referred to one skeptic about openness Richard Meyre at the Center for Disease Control. I don't know him. I just saw a document by him on the Web which expressed specifically concern about exactly that, the sharing of materials.

So although I agree with everything you've said there is no question that that is essential for the process of science. Nevertheless there are voices out there who see this as an issue.

DR. WARA: I have an implementation question for Dr. Reddy. I'm curious about why the Fink report recommended that the institutionally based IBCs are the first site to initiate the review of science funded protocols for risk of dual purpose.

Why not a more centralized group like the RAC?

DR. REPPY: Let me say I'm speaking just on my own behalf. The committee had many members and some of them might have a different view of why we did that.

But I think the argument that was persuasive was that first of all if you thought about the cost to institutions, there was a feeling that there had to be a local portal, that you couldn't centralize it in the sense of saying send everything to Washington and have them look at it.

Secondly, although I recognize that the IBC's where they're functioning are maybe already working about as hard as it's fair to ask people to do on a voluntary basis because these are your colleagues, after all, doing this work.

At the same time to say, well, we've got to have a whole other parallel system and make people run through both of them seemed even less efficient. So I guess I would say -- now, again, this is my personal opinion -- that what we did is we put this out as the suggestion with the hope that the

resources that the IBCs will need to do the job right would come from a recognition of how important the job is.

DR. FAUCI: It was also a question of practicality. It would be logistically almost impossible to have everything get referred to a central group. In fact, that's what we discussed, what the role of the NSABB would be. Should we handle everything that comes in or should we set principles for the Institutional Biosafety IBCs, and it was overwhelming that it should be done locally for a number of reasons, but for logistics alone would mandate that.

DR. WARA: And I agree with that. Tony, I'm wondering though. The principles that are set forth by this group then have to be sufficiently firm or robust so that they can be applied across IBCs at all the institutions, those who have significant resources, those who have none, those who are really experienced with research, those who have less experience.

DR. CASADEVALL: Although when you think

about that it makes sense in principle, I would ask the committee to also consider what has happened in clinical research where you could argue that the stringencies of the IRB process is basically slowing down clinical research.

So the point that we may now be at, the part of the curve where the regulation is really beginning to hinder progress. For the amount of science that we have and the amount of new products, their availability of reaching patients is disproportionately slow to the availability because the capacity is being strangled through the regulations, in my opinion, of clinical research, currently you have a very efficient process. It's still in basic science.

And as you put in the system, it has the potential for basically seeing what we see in clinical research, and I can tell you as a clinician it is very, very hard to move things through clinical research in the current environment, especially with the HIPAA Acts and a bunch of other acts and unintended consequences on the ability to translate

products into useful service.

DR. KEIM: I guess I would also point out with recombinant DNA there's some very specific guidelines currently for IRB committees, and a lot of research is exempted very early on because of these very detailed guidelines.

I think that's probably true in the clinical arena. We don't have anything like that in this arena yet at least.

DR. NICHOLSON: At the risk of getting into tomorrow's discussion a little bit about codes of conduct, you know, one of the aspects here that I think we may not have paid a whole lot of attention to is the Select Agent rule, and I will tell you it has struck me that maybe one of the outcomes maybe unintended of the Select Agent rule is that there is a very keen awareness on the part of the scientists of the seriousness of the materials that they have in their possession.

And I have seen a complete change at least at CDC -- I don't know about in other areas -- where the scientists really are very protective of their

work, and I think this is probably starting down a road that this Board could probably enhance.

DR. LEVY: Since the topic is communications, I wanted to overlap a little since Tony and Wendy are there in terms of what are we doing proactively to get the international scientific community aware of what's going on here and what will go forward?

Because I think the more that they're aware of the activities of the Board, and that could be a communication issue, the better we will be in understanding the task of making this an international effort. And so I just wondered. We should have learned by RAC who are the groups, the constituencies. I would assume they're the same.

But what can we do and what should we be doing to assure that we get the most from our efforts international?

DR. FAUCI: Stuart, it's an excellent question, and that will occur, but I think what we have to do is first understand ourselves, what we're doing. One of the risks of going out internationally

saying we have this NSABB and these are the kinds of things we want to do and our colleagues internationally as they almost certainly will do is ask for the kinds of fleshing out details of what we're going to be doing, and I think it's important to at least get some firm understanding and agreement of the broad strokes of the recommendations and the kinds of activities we'll be involved in and then to get the international community embraced with us rather than going out essentially in a very fuzzy way.

DR. LEVY: I do agree. I'm just wondering what is our base in terms of our knowledge of the international groups that will eventually be pulled in?

DR. FAUCI: Again, I can't give you chapter and verse of it. Maybe Amy does, but I would think, first of all, the international societies and the international academies is a very good place to start, which is, as you say, that ground has already been sowed with the RAC. So to me that's the most logical way to go. There are certainly others, but I think that's a good start.

MS. WHITE: It's hard to answer your question and not see you.

There are several levels of international community out there, and our European colleagues and others may be somewhat more organized to work with a Board like this. Many of our developing countries' scientists don't have any of the infrastructure needed to really respond, and I think there we need to work through the international organizations that are already set up.

This InterAcademy Panel which has a reach of 100 Academies of Sciences around the world, the International Council for Science, they're all in a position to really help reach into the developing world.

DR. REPPY: I think also though I'm perhaps guilty of it myself, that we shouldn't romanticize the history of RAC so much. It wasn't as if you waved a magic wand and had a working system. In connection with something else that I was writing I went back and read some of the contemporary reports of people and what happened at Asilomar and there was

obviously one hell of an argument. And I think that went on for quite a while and then closure was reached.

And now we have this sort of myth of how wonderful RAC is. I mean, we adopted it as a model which works, but I don't think we should underestimate the amount of work that went into that model, and I think you have to expect that you'll have to do that kind of work yourselves for this topic.

DR. COMELLA: I have to agree with several of the points that have been made in terms of international outreach. At this point it is important that there is a cohesive plan before reaching out to the international community.

At the same time I think they are all waiting to hear what the U.S. does have to say and what the U.S. can contribute. For example, recently the NSABB was presented at the Biological Weapons Convention Experts meeting, and all of the participants in the meeting, although states' parties, were quite intrigued by the idea of what we were doing in the U.S.

So I think there is international support, but at the same time, it has already been mentioned that there should be -- that this group actually should be thinking about international strategies both at an informal level through connections in scientific communities, but also consider how members here on this panel, such as the State Department, can help facilities reaching out to your international colleagues, whether in multi-lateral fora or in bilateral agreements and such.

So that is something that you should be thinking about as you move forward in planning and how to communicate dual use research to our international colleagues.

DR. RELMAN: I had a question for Tony Fauci. I think the notion of a culture of responsibility is so fundamentally important. And a large amount of our discussion so far has focused on a top-down approach, but as I know you know very well, it must also go bottom-up from the grassroots, and as a working scientist yourself, do you have some thoughts about how to win the hearts and minds of the

community, many of which may have at this point some degree of skepticism about the nature of this kind of endeavor?

DR. FAUCI: I have some ideas. I don't know whether they would work or not. I think, first of all, we need to not come out with pronouncements without vetting it out very, very carefully in the community. We've been given, the official members have been given the responsibility to come up with recommendations, and that will happen, but I think there needs to be a lot of discussion at the level, be they workshops or what have you, so that people really understand what it is that's happening.

As you all know, being part of the scientific community, David, that one thing people in academics don't like is dictation from above of what they do.

The other thing is the issue of threatening. There's a lot of anxiety about issues. I mean, I was a little chilled by your presentation. You were mentioning about herding cats. Could you imagine in a biological system academic setting to

have an E-mail checked by somebody. I think that would be the end of that very quickly.

So what I would say is that we would probably need to be very transparent about where we're going as we're getting information because we really don't want to have a situation where they feel threatened in their independence, threatened in their ability to pursue their own academic pursuits. We've got to make that very, very clear.

And that I think is inherent to the concept of a culture of responsibility. The culture of responsibility presupposes that you're going to act on your own and be your own person in the pursuit of knowledge, and that's why you need the responsibility.

So I think we need to keep hammering that in.

DR. PATTERSON: I just wanted to respond to several comments that have been brought out about the need for this committee to think about the dual use issue in an international way, and as has been previously mentioned by the chair. We will be forming among our five subcommittees. One of them is devoted

precisely to that, to thinking about the international landscape, to promote strategies for international collaboration.

And one of the first tasks that that subcommittee will be to look at a full inventory of the activities that are already well underway or just beginning globally.

So we appreciate your comments and will take them to heart.

GEN. GORDON: Phil commented earlier on the lack of an interjournal mechanism for coordination and security issues. I wonder if you could just expand on that in a couple of sentences. Is it useful? Is it practical?

DR. CAMPBELL: You mean increased collaboration between journals?

GEN. GORDON: I think, if I understood your comments, with respect to sort of the review issues, there was no way to pass that among journals or to coordinate among journals. Would that be useful or would it in fact be practical?

DR. CAMPBELL: I think if you had a

situation where the paper had been rejected for purely security reasons and you had a feeling that this could well be submitted to other journals of the same ilk, you could tell a few people, but the idea that you would have a registration set up that would cover every journal in the world, for example, would as far as I'm concerned be totally impractical.

So I do have a problem with that idea.

DR. ERLICK: I would just make a comment in general. I think it's absolutely critical that because this is the national Board that we have a buy-in from our colleagues throughout the whole research sector. If we don't I don't think we're going to succeed, and I know there's skepticism out there right now because it is, again, the government, and I think we need to make our colleagues, as I think we're going to do, a part of the process and have a buy-in nationally and ultimately internationally.

ADM. STUDEMAN: I was trying to capsulize what I think are the most important strategic messages based on the presentations and the questions asked in the last hour and a half or so, and if I articulated

them back in a certain kind of way here, maybe I could get the panel to comment on them.

One is I think sort of there's general enjoyment that the whole objective here is to stay ahead of the curve, whatever the curve is, and that clearly some sense of offense and openness and defensive mix is kind of required here.

I got the sense from the presentations that most people think in this particular area the genie is already out of the bottle and that it's only going to get worse in terms of the genie essentially being out of the bottle, but that perhaps some defense is required, how much to pursue, to blunt, or to catch the incompetent, the inadvertent. To raise the sensitivities is important or to slow down the process to buy time is some sort of strategic factor here, but that, again, offense and openness, that is, research to blunt whatever might come in the future is an important factor here, or to focus on specific threats if we're able to do that at some point or other processes that we haven't yet discovered.

That's sort of a general capsule or

rundown of what I seem to be getting out of this from the point of view of strategic messaging, which I'm still trying to interpret.

I think there's a question there somewhere.

DR. KEIM: You know, one of the things that seems very -- I mean, some of these things it seems like we can do. You know, we can have individual journals have some type of a review process. We can have IRBs check the box. We're going to look at your proposal.

We're going to have investigators even keeping track of this.

But what dual use is is always going to be a moving target for us, and it seems like at some point we're going to need to have a group that is helping to decide what dual use is on a case-by-case basis, on a day-by-day basis, and in what the context is because the context is going to be continually changing and so this isn't going to be something that we can say if it's E. coli K-12 it's okay.

It's going to be something we're going to

have to redefine on a regular basis, I'm afraid.

DR. FAUCI: Phil, I'd like to ask you a question. I really enjoyed your presentation and the scope and the thought of it, but if the process works, of the culture of responsibility that's translated to the IBC through principles that come from the NSABB, an experiment itself may be discouraged being done if it turns out to be something that might be a serious issue.

But if it goes through the process well, can you conceive of in the biological sciences any piece of work that you feel shouldn't be published?

DR. CAMPBELL: I'm going to reveal to the world that this is a question that I asked him some way back.

(Laughter.)

DR. CAMPBELL: The answer was no or the answer was almost no, and I never discovered what it was that he thought you should conceal.

I mean, the answer is no when it comes to the basic research, and the phrase that we used before about the genie being out of the bottle, you know,

that has to be the case with basic research, as far as I'm concerned.

But at the same time, the weaponization questions, the questions about some of the papers we talked about, the Botulinum toxin sort of paper, the polio synthesis sort of a paper, those are papers where I think you can have a genuine debate about whether they should be published or whether they should be published in the way they were published.

And so the question is where do you shade off between the extreme case of a weaponization recipe and the basics, and this is the first group of people who have gathered together with the specific job of addressing that, and I await their deliberations.

DR. FAUCI: Actually just to get back to our previous discussions, I agree with you completely. When I look at fundamental basic, I find it very, very difficult to come to a conclusion of something that you should hold back.

When you're talking about a recipe to do something, that's when it's pretty clear that you've got to be careful about that. How you make this or

how you do this, which is the reason why the botulism story really generated appropriately a lot of discussion.

DR. ROTH: I really like the idea of the culture of responsibility. I think that has to be the key, and having IBCs take that responsibility.

We also have to be careful that IBCs can be different and some people might take that responsibility too zealously. So we have to be pretty clear on what things need scrutiny so that they don't over interpret the responsibility and shut down too much research at that early stage.

DR. NIGHTINGALE: Yes. Thank you.

I have a question for Dr. Campbell.

You have a system set up already for review. It sounds like a reasonable approach. If we were to say what could this body do to help you at this point in time, what would your answer be? What kind of activities could we do that would be of assistance?

DR. CAMPBELL: One thing you could do is give to us a list of other possible sources of advice,

and you might even want to consider whether there is a public source of advice, not about the individual consultations we would make, but in terms of a publicly acknowledged group of people who are willing to be consulted by journals more generally.

DR. CASADEVALL: I think Dr. Fauci began to hit it. I mean, in a way crystallize his comments is crystallize what one might be imagining, not as a line on the sand, but maybe a little bit, and that is weaponization is a form of applied research. At that point you're taking something, and you want to figure out how to disseminate spores. You want to figure out how to defeat a vaccine. You are already applying the basic science to do something with it.

Whereas the basic science may be dual use, but it's very difficult initially, a priori to restrict it, whereas once you begin to cross into the application, then you may be at the beginning of an emerging distinction between what we want to come to grips with.

DR. OSTERHOLM: I think one of the issues though that we're dealing with here today is still

trying to get our arms around what is it that we really are concerned about, and I come back to our earlier comments, that what happens at Los Alamos is so unlikely to ever be a major problem because you have to have access to the material; you have to have a way to deliver it; and you put this all together.

Given the security you have, one wouldn't necessarily say it's overkill, but on the other hand, you could say that it would be very difficult even if you didn't have a level of security to execute some type of adverse event, a terrorism event based on that.

I think for us what we're trying to get our arms around is that there are many, many possibilities to do something bad with biologic agents that are relatively easy to do. I mean, we've given you examples already, and I would add it's interesting to note that of all the ones I'm aware of in this country, they obviously have either been food or have been through the mail. I won't comment on the anthrax situation not knowing, but basically they've all been domestic sources. None of them have been

international in source.

And I think that what we have to start taking a step back at is ask ourselves, again, what is it we're really trying to do here. I mean, is it trying to keep the Shigella out of the salad in the dales in Oregon? Is it we're trying to stop the anthrax spore that's been built, that's been put together from being disseminated?

And any of those are going to have a very different level of scrutiny or control, and I would hate to see us trying to run laboratories and publications and public health around the issue of Shigella in the salad bar, which I would argue there's been so many real experiences, that if somebody published on that, that wouldn't be of concern to me.

If somebody published on something else, it could be a concern, and so I think part of what we're trying to do is work this, and I don't think that's going to come right away. I think it's going to take time going through and taking scenarios and beginning to understand what do they mean to us and is this a problem or not.

So I fear that we're going to try to come out of here with this is dual use. This is what we should be concerned about. This isn't what we should be concerned about. I think it's going to have a lot of common sense applied do it, and that's why I think it comes up locally.

I think locally we're going to have to have people who are basically arm's length away saying, "Now, have we thought about all of these things? Are these the possibilities?"

The last thing I just want to say is I just have a bias here, and I know this will go against the grain here. There is no such thing as a weaponized biologic agent. It doesn't exist. It's a misnomer of terms.

Any biologic agent can be weaponized. Foot and mouth disease virus today is a weaponized agent if you want to use that term by merely just bringing in sample from a foreign country in a little baggie and releasing it in the barnyard.

Even anthrax is not in a sense weaponized. It's all about the combination of the bug and the way

to deliver it, and any of those -- and I made the point earlier on a given bug. If it doesn't have a way to be delivered, it isn't really a, quote, unquote, serious problem. A bug that may not be real bad but with efficient delivery to a lot of people could be a bad thing.

And so I think we have to be careful, too, because I hear that terminology, and unless somebody can convince me differently and they haven't been able to in four years, there is no such thing as a weaponized agent.

There may be agents with more pathogenicity or virulence, which is an agent-host combination. It's not the bug. It's both.

And I think that that's what we have to understand because that's going to get us, I think, in trouble if we try to really focus on weaponized agents.

DR. KEIM: And we're not going to convince you today, Mike.

This is going to wrap up this portion of this session and we're going to move now into the

public comment stage. This stage will last for only 35 minutes.

If you've registered, it's time now for our audience members that have registered to make public comments. This session will be 35 minutes in length. I will ask the public to keep your comments brief and to the point. We're going to limit the public comments to three minutes individually.

When I call your name please approach the microphone and address the Board. At the three minute mark I will ask you to stop and give you just a few seconds to finish up and summarize, but at that point then it will be time to move on to the next speaker.

Our first public comment will come from Shenne Chiao, M.D. from Washington, University in St. Louis.

DR. CHIAO: Okay. I represent Midwest Regional Center of Excellence for Biodefense and Emerging Infectious Disease Research.

My comments are while biosafety and biosecurity share many features, there are significant differences. Biosafety primarily focuses on

occupational health and environmental protection. Biosecurity, on the other hand, focuses on public health and the national security.

Thus the potential impact of failure is much broader than in biosecurity. As a result of these differences, the existing strategy of compliance with NIH guidelines, which includes risk assessment by the institutional biosafety committee and primary investigator documentation and training, may not be sufficient to deal adequately with biosecurity issues.

Developing additional strategies is essential. We believe this additional strategy should focus on culture change in biological research community in terms of biosecurity. Biosecurity precautions and procedures should become part of daily activities for everyone who works in the laboratory.

To change this culture can often be a challenge, especially to those who are highly educated and endowed with a strong scientific mind, but it can be done.

The most effective way to accomplish this culture change is through education, just as proposed

by NSABB. A mandatory education program for all scientists and the lab workers and, in our opinion, graduate students, should also be considered.

Additionally, a strong partnership between science and the regulatory communities should be developed. A scientific survey and data analysis should be incorporated into the policy. And we should implement a feed back system to monitor progress.

In this age of bioterrorism and wide availability of biotechnology, it is long overdue for the science community to change its culture in terms of biosecurity and adapt itself to this threat.

Thank you.

DR. KEIM: Thank you.

Dr. Gerald Epstein from the Center for Strategic and International Studies.

DR. EPSTEIN: Thank you for the opportunity to address you.

This has been a fascinating meeting. You all recognize there's no body or institution that does anything like what you are here to do, and I've been following the discussion of how we're trying to grope

with what's the Board's mission, what's in, what's out, and I heard two attempts at trying to find things that we don't have to do. We've done a very hard job. So let's find things you don't have to do.

One is there's a whole set area where it's too late to change. The genie is out of the bottle. We don't need to look there.

We have another set of discussions about basic fundamental research. It's too early to tell. We really don't know enough to add any value there.

And I think where you need to focus is to look for something which might actually be in between. It may be possible there. There are things that are not both at the same time. If it is both too early to tell and too late to change, there is not a lot of value in working at it, but I submit that not everything falls in that category.

And when I've been trying to think through this topic of what are we actually trying to get at, the definition I came up with which I think is right before you I called contentious research, and I define that to be fundamental biological or biomedical

investigations that produce organisms or knowledge that could have immediate weapons and locations and, that, therefore raise questions concerning whether and how the research should be conducted and disseminated.

This is my operational definition of what the "it" is. It's not a set of criteria or experiments of concern that tell you what is and what isn't out of your purview. It's operational. It raises questions.

And there are two kinds of questions. There are questions that are well founded. Should this work be done? Should it be published? Is there more harm than good, difficult as it may be to come to that assessment? But is there a real reason why we should think seriously before going ahead and doing something?

That's a legitimate question. But in a society where research is funded by public dollars and tolerated by public consent, there are also questions that may actually not be in some sense well founded on a technical basis, but they're questions that people have.

And I would suggest that if research is done and it raises questions and gets people worried and gets the political system alarmed, that is something that you have to worry about, whether or not that question is one which you think is well founded.

And it is your responsibility or let me up it a little; it is the scientific community's responsibility working with many other stakeholders to have answers to those questions. The answer may be that's a good question. We've thought about it, and here's the process we have in place and here's why even though it's pretty scary to go down this road, it's more dangerous not to than to do it.

That's an answer. It may not convince everybody, but it's a lot better than science is pure, it has no good or bad. We don't ask that question. We just go ahead.

I used to work for an agency of the U.S. Congress, and I used to say Congress is a blunt instrument. I used to say they've got a big red button and a big green button. Now I would say they've got a big red button and a little green

button, but that's the way to get the red button slammed.

If science looks like it's going ahead, saying these issues are not under our purview; it's not our concern, that button is going to get hit. So I think this Board's job along with the scientific community is to make sure we have answers when questions are raised.

I want to thank each one of you for serving on this Board. It's a real hard job, and I'm very glad you've taken the time from your schedules to do it.

Thank you.

DR. KEIM: Thank you.

Our next public commentator is Ed Hammond from the Sunshine Project.

MR. HAMMOND: Thank you for the opportunity to speak.

I have two comments, the first of which will be brief. It's something that I observed at the beginning of the meeting.

In my understanding the inside was to have

public members, and unless I missed it I didn't see a public member or members on the Board. And I think that that would be a useful thing to incorporate because organizations like mine and other public commenters can work through public members to try to raise concerns. So I would appreciate a clarification on that.

Secondly, my major purpose in asking for the floor was to introduce this paper, a copy of which I've provided to each of the members of the Board, and which I hope you might be somewhat familiar with already. It's "The Mandate for Failure of the State of IBCs in an Age of Biological Weapons Research."

It has been covered in Science and the Chronicle of Higher Education.

This is a survey that the Sunshine Project did last year of almost 90 percent of registered IBCs in the U.S. It was intended to be a study of transparency. What we were looking at was trying to assess how fear about bioterrorism was impacting disclosure of information by IBCs.

What we discovered was something far more

disturbing than what we intended, which was a debate over transparency. What we discovered was that in large measure, although there are many exceptions, but in large measure the IBC system is something of a fiction.

And I think that this shows that the NRC was somewhat incautious or arguably erred in the Fink report in recommending local review, not because local review in and of itself is bad, is a bad idea, but because the system there to perform the reviews is in a very sad stage.

We found widespread disregard, widespread noncompliance with the NIH guidelines. For example, the first experiments to insert 1918 genes into influenza went ahead without IBC review despite USDA, HHS, DOE, DOD regulations, rules, contracts, et cetera, requiring compliance with the NIH guidelines. Sixty percent of government IBCs did not provide their minutes.

We had an institution that had approved four dozen research protocols, including Select Agents at BSL-3 and recombinant DNA, and their IBC had never

met, but somehow had approved four dozen research protocols.

We generously estimate that ten percent of the private sector is compliant with the NIH guidelines and has a registered IBC. We found many IBCs that have never met once, maybe twice.

I could go on and on and on and on. And sadly, don't interpret this the wrong way. It includes most of the institutions that are represented on the podium before me. I found problems with the IBCs.

So the bottom line is no matter how brilliantly and now matter how well you do your job, and I want to emphasize that at least speaking for myself, I have a very open mind and welcome this effort; the bottom line is that the local committee system that you're relying on is failing at its present mandate, and to heap this mandate on top of it poses some serious problems.

So you will have to devote considerable attention to making sure that these IBCs actually exist, comply with what you recommend, and that there

is a real bona fide process of review going on for those experiments that require local review.

I think a significant number should require national review, and I'm being told that my time is up.

So thank you very much for the opportunity.

DR. KEIM: Thank you, Mr. Hammond.

So next on our speaker list is Brian Hanley from the BW Education and Forensics. That's the only title I have. Mr. Hanley.

MR. HANLEY: Yes. I want to primarily comment that there's kind of a pervasive sort of back follow thing where you guys are talking about addressing a biological weapons problem and yet we are extremely naive about biological weapons in general, and I think most of the people here are.

I'm coming at this from the attack side, from having done a serious red team scenario including simulation, et cetera, and what I would say on a specific basis is two things.

One is of all the things that came to me

as I did this, the primary thing that I see us having a shot at controlling, which actually requires serious expensive resources, is controlling access to very sophisticated simulations, such as EpiSims.

And I'll point out that NIH allocated a grant this February to make EpiSims public domain in its source code, and I would very strongly disagree with that. It has accurate demographics for American cities. It has GIS. It's very sophisticated, and it will allow you to war game if you turn it around. So that's one very simple thing.

The other one is that in doing this exercise, what became clear to me is that your primary problem becomes how do you know something is happening, and currently we depend on extreme symptoms, and we depend on people dying in order to know that. We're very unsophisticated that way.

I would point to the Viral Defense Foundation's proposal which some of you may be familiar with, to use blood serum, to continuously survey what viruses are in circulation so that we start finding out about true morbidity and so we start

finding out what the background really is so that if something shows up that's odd, we'll see it.

And I'll also point out that relative to whether or not we have engineered or, you know, natural terrorist kind of organisms that appear, you want to do the same thing in either case, and that becomes your primary biodefense because if you don't know what's happening you can't respond.

And I'll close by saying I think the primary focus of this Board should be far less on control of what gets published and far more on focus on what research needs to be done and where to direct things because scientists are not the problem. You guys are going to be the ones who are going to direct the people who are going to be able to address these issues if they can be clarified.

DR. KEIM: Thank you, Mr. Hanley.

So next on our list is Robert Harris from Masimax Resources. Robert Harris.

Okay. I'll give him to the count of three.

All right. We'll move along then. The

next on the list is David Silberman from Stanford University.

MR. SILBERMAN: In addition to my other roles, I'm also the community member to the UCSF Biosafety Panel, an active participant at Stanford's IBC, and in my day job, I direct the health and safety program at the School of Medicine at Stanford University, which includes a lot of compliance related issues.

Some of the observations I've made is that when you're dealing with a guideline or a regulatory concept in a large and diverse community, it's always a good idea to look backward and see what has worked in the past. I think it's to our credit that Asilomar has come up, and I should note that this is the 30th anniversary year of that conference.

But in addition, in health and safety we have other concepts, one of which is known as performance based standards, something that has worked by experience. No one has dictated it. It's just one of those things that fell out.

We look to that for a reference point, and

that's not to say that we don't try to refine it, but it's a place to start. And I would urge you to consider that.

Also, in dealing with investigators and principal investigators, they respond more toward reason than regulation, more towards guidance than dictation, and I think that's pretty clear.

But I would urge you to also consult the individuals within the institution who are charged with the responsibility of making sure that we are in compliance from the humble biosafety officer to the exalted vice provost for health and safety. There's a lot of people who know how to work with faculty.

I should say we have our ways. Isn't that right?

Okay. And one other comment about balance. A lot of discussion is focused on balance, and I would urge you to think that it isn't necessary for the fulcrum to always be in the middle. Sometimes it can be at the extreme end and you will still have balance where you have a lot of research, a lot of science, and only a modicum of security, but that

balance does exist. So please take that into account. You don't need a lot to offset a lot.

I'll conclude my remarks at that.

DR. KEIM: Thank you.

Our final public speaker is Terence Taylor from the International Council for the Life Sciences.

Terence.

DR. TAYLOR: Thank you very much.

And I'm very pleased to have been given the opportunity to address the NSABB.

I come from the International Institute for Strategic Studies, whose membership reaches out to over 100 countries around the world, and I have the good fortune to head the U.S. office of that organization, and with other partners here in Washington in the Chemical and Biological Arms Control Institute, we have developed with funding support from the Nuclear Threat Initiative on their global health and security program the International Council for Life Sciences, a charter based organization.

I'm impressed by what I've heard today because the centerpiece of our work and the

inspiration for me in undertaking this project was very much that the focus should be on people and knowledge in the life sciences area, and that's hugely important.

And the second phrase which we've heard from the beginning from Dr. Zerhouni and later from Dr. Fauci and others, that our mantra when we began this project was the culture of responsibility, and I'll tell you why: because drawing on Dr. Stuart Levy's remarks at the beginning, is that we should take a positive approach. With the culture of responsibility idea, in my view you're pushing on a door that's already open.

And our work around the world with this project is that the overwhelming majority of scientists working in this area, whether it's in industry or whether it's in government institutions or in academic places, want to behave responsibly.

And I'm not looking at the world through rose colored spectacles because I was also a weapons inspector and interviewed people, including Dr. Rahid Taha whom you saw in the photograph earlier on, and

she represents one end of the spectrum.

But the overwhelming majority of people that I have interacted with with this project and previously will buy this idea of a culture of responsibility, and I was delighted to hear that repeatedly today, and that underlined our project.

It is clear that this question of balance, it's clear that the advances in the life sciences are bringing and will in the future bring enormous benefits, and that's another plank on which to build, particularly in the international realm because this council that we have set up, I think, is directly responsive to that activity that you have, and I think you used the word "coordination of international research." I think a better might be "harmonization of international research." I think "coordination" is perhaps very ambitious.

And so I think one needs to think about the idea which we have in our mission statement which, Mr. Chairman, you have a copy of our charter with you. Our mission statement is about promoting best practices and promoting codes of conduct.

Because we believe that there will not be one global code of conduct that will operate over every professional area and also in every region of the world. What we have created is a charter which forms the structure under which a number of codes of conduct applicable in professional societies around the world, that they could operate against.

And so I think I would urge you to have a look at our charter and our organization stands ready to support you in your work, particularly on this international outreach aspect because I think you have to take that in from the beginning in terms of obviously you have to work things out internally and how they're thinking around the world from the beginning.

Thank you.

DR. KEIM: Thank you, Dr. Taylor. We hope to see you tomorrow when we're discussing international issues.

So I hope all of you have found the information presented today as valuable as I have. Lots of interesting discussion and good points being

made.

On behalf of the Board, I would like to thank Dr. Zerhouni and Dr. Fauci for their comments in support of this Board. I'd also like to thank the audience for joining us today.

It is apparent from the turnout that biosecurity is a subject that many people are interested in discussing.

Finally, I'd like to express my gratitude to the speakers for traveling to Bethesda to share their insights and expertise with us. You really have spiced things up for us today and given us new insights.

Tomorrow we will begin the sessions at 8:00 a.m. The sessions will be code of conduct and the life sciences.

The second session will be dual use research, international perspectives.

And finally, the chemical synthesis of bacterial and viral genomes.

With that, I'll adjourn the session for today and hope to see you tomorrow.

(Whereupon, at 5:47 p.m., the meeting was adjourned, to reconvene at 8:00 a.m., Friday, July 1, 2005.)