AUTHENTICATED
U.S. GOVERNMENT
INFORMATION
GPO

S. HRG. 109–111

BIODEFENSE: NEXT STEPS

HEARING

BEFORE THE

SUBCOMMITTEE ON BIOTERRORISM AND PUBLIC HEALTH PREPAREDNESS

OF THE

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS
UNITED STATES SENATE

ONE HUNDRED NINTH CONGRESS

FIRST SESSION

ON

EXAMINING THE BIODEFENSE RESEARCH PROGRAM OF THE NATIONAL INSTITUTES OF HEALTH, FOCUSING ON THE DEVELOPMENT OF MEDICAL COUNTERMEASURES AGAINST A BIOTERRORIST ATTACK

FEBRUARY 8, 2005

Printed for the use of the Committee on Health, Education, Labor, and Pensions

U.S. GOVERNMENT PRINTING OFFICE

98–930 PDF WASHINGTON : 2005

For sale by the Superintendent of Documents, U.S. Government Printing Office
Internet: bookstore.gpo.gov Phone: toll free (866) 512–1800; DC area (202) 512–1800
Fax: (202) 512–2250 Mail: Stop SSOP, Washington, DC 20402–0001

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS

MICHAEL B. ENZI, Wyoming, *Chairman*

JUDD GREGG, New Hampshire
BILL FRIST, Tennessee
LAMAR ALEXANDER, Tennessee
RICHARD BURR, North Carolina
JOHNNY ISAKSON, Georgia
MIKE DEWINE, Ohio
JOHN ENSIGN, Nevada
ORRIN G. HATCH, Utah
JEFF SESSIONS, Alabama
PAT ROBERTS, Kansas

EDWARD M. KENNEDY, Massachusetts
CHRISTOPHER J. DODD, Connecticut
TOM HARKIN, Iowa
BARBARA A. MIKULSKI, Maryland
JAMES M. JEFFORDS (I), Vermont
JEFF BINGAMAN, New Mexico
PATTY MURRAY, Washington
JACK REED, Rhode Island
HILLARY RODHAM CLINTON, New York

KATHERINE BRUNETT MCGUIRE, *Staff Director*
J. MICHAEL MYERS, *Minority Staff Director and Chief Counsel*

SUBCOMMITTEE ON BIOTERRORISM AND PUBLIC HEALTH PREPAREDNESS

RICHARD BURR, North Carolina, *Chairman*

JUDD GREGG, New Hampshire
BILL FRIST, Tennessee
LAMAR ALEXANDER, Tennessee
MIKE DEWINE, Ohio
JOHN ENSIGN, Nevada
ORRIN G. HATCH, Utah
PAT ROBERTS, Kansas
MICHAEL B. ENZI, Wyoming (ex officio)

EDWARD M. KENNEDY, Massachusetts
CHRISTOPHER J. DODD, Connecticut
TOM HARKIN, Iowa
BARBARA A. MIKULSKI, Maryland
JEFF BINGAMAN, New Mexico
PATTY MURRAY, Washington
JACK REED, Rhode Island

ROBERT KADLEC, M.D., *Staff Director*
DAVID C. BOWEN, *Minority Staff Director*

C O N T E N T S

STATEMENTS

TUESDAY, FEBRUARY 8, 2005

	Page
Burr, Hon. Richard, Chairman, Subcommittee on Bioterrorism and Public Health Preparedness, opening statement	1
Kennedy, Hon. Edward M., a U.S. Senator from the State of Massachusetts, opening statement	3
Enzi, Hon. Michael B., Chairman, Commmittee on Health, Education, Labor, and Pensions, prepared statement	4
Roberts, Hon. Pat, a U.S. Senator from the State of Kansas, prepared statement	6
Fauci, Anthony, M.D., Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, U.S. Department of Health and Human Services; Penrose C. Albright, Ph.D., Assistant Secretary for Science and Technology, Department of Homeland Security	7
Prepared statements of:	
Anthony Fauci, M.D.	10
Penrose C. Albright, Ph.D.	22
Painter, George, Ph.D., CEO, Chimerix, INC.; Jon Abramson, M.D., Professor and Chair, Department of Pediatrics, Wake Forest University School of Medicine, Winston-Salem, North Carolina; Gerald L. Epstein, Senior Fellow for Science and Security, Homeland Security Program, Center for Strategic and International Studies; Gordon Cameron, CEO, Acambis, PLC	46
Prepared statements of:	
George Painter, Ph.D.	49
Jon Abramson, M.D.	54
Gerald L. Epstein	60
Gordon Cameron	70

ADDITIONAL MATERIAL

Statements, articles, publications, letters, etc.:	
Summary of the President's 2006 budget for Homeland Security	31
Questions of Senator Roberts to Mr. Albright, Ph.D.	37
Questions of Senator Roberts to the panel	37
Questions of Senator Enzi to Mr. Albright, Ph.D.	44
Generic Pharmaceutical Association	82
Randi Airola	84
Meryl Nass, M.D.	87
The Military Vaccine Education Center	91

BIODEFENSE: NEXT STEPS

TUESDAY, FEBRUARY 8, 2005

U.S. SENATE,
SUBCOMMITTEE ON BIOTERRORISM AND PUBLIC HEALTH PREPAREDNESS, COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The subcommittee met, pursuant to notice, at 10:05 a.m., in room SD–430, Dirksen Senate Office Building, Hon. Richard Burr, chairman of the subcommittee, presiding.

Present: Senators Burr, Roberts, Enzi [ex officio], Kennedy, Murray and Reed.

OPENING STATEMENT OF SENATOR BURR

Senator BURR. I would ask that the subcommittee hearing come to order. I want to thank you for coming to the first hearing of the Health Subcommittee on Bioterrorism and Public Health Preparedness. I am looking forward to working with the chairman of the full committee, Senator Enzi, the ranking member, Senator Kennedy, and all the members of this subcommittee throughout this session of Congress.

I think that we have the distinction of holding the first Health subcommittee hearing of the year, but I have always believed that when it comes to bioterrorism, you have to be ahead of the curve. Already the Senate has before it S. 3, the Bioterrorism Legislation, introduced by Senator Gregg. I know that Senator Hatch and Senator Lieberman have also been working hard on a Bioshield II bill.

Bioterrorism has been an important issue to me for some time. In fact, I sponsored the first bioterrorism legislation in the House before September 11. It was obvious to me the United States had a very real vulnerability to being held hostage to bioterror. After September 11, it became even more apparent that the threat was real and the government needed to work with industry to build up our protection and our ability to react to any type of an attack.

As a freshman senator, I recognized that many senators before me have worked very hard on strengthening our Nation's defense against bioterrorist attacks. I am humbled to have the opportunity to work with them and many of whom are members of this committee and specifically this subcommittee.

As I mentioned earlier, as a member of the House of Representatives, I sponsored the first bioterrorism legislation in the House, the Public Health Threats and Emergency Act of 2000. I was pleased to help create the Public Health Security and Bioterrorism

Preparedness Response Act of 2002, and followed that legislation up with the Smallpox Emergency Personnel Protection Act of 2003.

This subcommittee has a lot of important work ahead of it. Last year, the Project Bioshield Act was signed into law, but many people believe that there is a need for subsequent legislation that will further strengthen the program's viability. This year we will take up that discussion and legislative action on this important subject.

Next year, unbelievably, it will be time to reauthorize the bioterrorism legislation from 2002. The goal of today's hearing is to examine implementation of Project Bioshield. I believe that Bioshield has begun to address the bioterrorism threat but acknowledge that more is needed to fully protect our country. In order to increase critical scientific effort in the area of the bioterrorism preparedness, the government must have full participation in this work from the pharmaceutical and biologic industries.

I hope that today's witnesses will help us understand what we can do, what industry can do, to achieve the best working relationship that benefits the American people.

Our first panel we have Dr. Tony Fauci, Director of the National Institute of Allergy and Infectious Diseases. Dr. Fauci is the lead scientist and director of the HHS effort on bioterrorism.

We also have Penrose Albright, Assistant Secretary of Science and Technology Directorate at the Department of Homeland Security. Mr. Albright has been involved in the national security arena since 1986 and is directly involved in the implementation of Project Bioshield at the Department of Homeland Security.

On our second panel, we have Gerald Epstein, a Senior Fellow for Science and Security at the Centers for Strategic and International Studies, Homeland Security Program. Mr. Epstein will give us a broad overview of bioshield implementation and the private sector's reaction to the law.

We have Mr. Gordon Cameron, CEO of Acambis. Acambis is a successful biotechnology company with facilities in Massachusetts. Acambis has produced a smallpox vaccine and will give us their perspective of the research field pre-Bioshield and any changes that need to be made since then.

I am especially pleased to introduce the next two witnesses who are from North Carolina. The main reason they are speaking today is they are experts in their field. It is just particularly nice for me that North Carolina has some experts that I can have testify. Dr. Jon Abramson is the chair of Pediatrics at Wake Forest Baptist Medical Center. He is a member of the CDC's Advisory Committee on Immunization Practices. Dr. Abramson will talk about the need to increase liability production for pharmaceutical and biologic companies involved in the areas of research.

Mr. George Painter is the president and CEO of Chimerix, a small biotech company in North Carolina's Research Triangle Park. Mr. Painter will talk about the additional research tools and coordination needed by pharmaceutical and biotechnology companies in order to successfully produce bioterrorism countermeasures.

I thank all of our witnesses for their attendance today. We look forward anxiously to your testimony. I thank the chairman and at this time I would recognize the ranking member, Senator Kennedy.

STATEMENT OF HON. EDWARD KENNEDY, A UNITED STATES SENATOR FROM THE STATE OF MASSACHUSETTS

Senator KENNEDY. Thank you very much, Mr. Chairman. The first meeting of a new subcommittee is always an important occasion. I particularly commend our full committee chairman, Senator Enzi, for his decision to devote a subcommittee to the issue of defense against biological attacks, and I also commend our subcommittee chair, Senator Burr, for an impressive record of accomplishment already on this issue. We are off to a good bipartisan start.

Five years ago Senator Frist and I worked with Senator Burr when he was a member of the House on the first legislation to deal with the public health defenses against bioterrorist attack. That measure was signed into law a year before September 11, and in the wake of that attack, a more extensive bill on the issue was enacted in 2002.

Senator Burr contributed important provisions in that bill. We also worked together on the compensation program for persons injured by smallpox vaccine, and his leadership will serve the Senate and the country well in all aspects of this issue.

The Nation is obviously vulnerable to attacks with weapons of mass destruction. Our focus today is developing new medical initiatives in the fight to keep American families safe. We must also recognize that even the best new treatments will do little good if our emergency rooms are so overburdened that doctors and nurses cannot deliver the effective care. The most modern disease monitoring system will be of little use if public health agencies are so starved for funds, they cannot keep their community safe.

I want to just mention on the budget matter, we have seen the proposed cut in funding from 2005 to 2006 in the CDC program. We have the two aspects of the CDC program which are well known and understood. First of all, you have to have the detection, which the public health system does, and then you have to have the treatment and the containment, which the hospitals do. The cuts impact the CDC program that has been working with the health agencies that do the detection and the hospitals for the containment. And that is all part of this whole effort to deal with the problems of bioterrorism. So this is certainly something of very considerable concern to many of us.

Study after study has shown that health agencies and hospitals are making progress, but it is very slow, and they have a long way to go. Despite the clear need for greater Federal aid, the budget contains a 12 percent cutback in the Federal programs that strengthen the health agencies, a major cut in the program to strengthen our hospitals.

We took a significant step in Bioshield in the last Congress to develop the cures of the future, but will slide back if these proposed cuts are allowed to take effect. Our committee has received many proposals to improve Bioshield through additional incentives to industry. Incentives are an indispensable part of defending against bioterrorism, but the incentives have to be appropriate. We cannot afford to squander resources on needless giveaways.

We are hearing today from a drug industry executive who is doing the right thing, Gordon Cameron, who is the CEO of Acambis

to whom America owes a great debt of gratitude for what Acambis did in producing 180 million doses of vaccine to keep the Nation safe from smallpox.

I hope the administration will build on this success by providing the funds needed to keep the production line for smallpox active. What did it take to get Acambis to complete this essential project? No wildcard patent extension, no extra market exclusivity; it was just a contract under which Acambis produced the vaccine on time and on budget. Obviously we need to examine how Bioshield achieves its objectives, but we should not run into overturning a balanced system of patent incentives in the name of biodefense.

A similar issue arises in cases where some patients may be harmed by the product itself. As part of the smallpox vaccination effort, Congress granted appropriate indemnity for the manufacture of the vaccine and the health professionals who administer it. That indemnity was justified in the case of smallpox since the vaccine could not be fully tested or meet FDA standards at the time. Targeted indemnity protections make sense, but that does not mean broad exemptions for negligence just because the products have value for biodefense.

It is also important to have fair compensation for persons injured by faulty products and proper safety protection for the workers who administer them.

I look forward to the testimony of our witnesses that are working with my colleagues to consider these issues and making genuine improvements that might be needed in Bioshield. I thank the chair very much.

Senator BURR. Thank you, Senator Kennedy. At this time the chair would recognize the full committee chairman, Senator Enzi.

The CHAIRMAN. Thank you, Mr. Chairman, and I would just ask that my statement be made a part of the record as well as anybody else who wants to make a statement to keep in the tradition of having the chair and the ranking member do the statements. I do appreciate all the expertise that you bring to this and am so pleased that you are the chairman and are taking this careful look at the impediments that are out there to the current system. It was not perfect, but we got it done. The next one will not be perfect either, but we will get it done, and I appreciate the work you are going to do.

Senator BURR. I thank the chairman. Without objection, all opening statements will be made a part of the record.

[The prepared statement of Senator Enzi follows:]

PREPARED STATEMENT OF SENATOR ENZI

The threat of infectious disease spread by an epidemic or bioterrorism is one of the greatest dangers currently facing us as a Nation. As great a danger as it is, however, it is dwarfed by our largely untapped ability to experiment, innovate, and deliver the next generation of diagnostics, vaccines, and therapeutics to address it.

That is why I greatly appreciate Chairman Burr's willingness to hold this hearing and begin the work we must do if we are to have an effective plan in place before it is needed. I am looking forward to working with him, other members and stakeholders in the

months to come on this and many other issues of concern that will have a great impact on our Nation's safety and security for a long time to come.

Today's issue of Biodefense can't help but call to mind the days so many of us spent as Boy Scouts. We all had Scoutmasters who drilled into us the importance of the Boy Scout motto—Be Prepared! Since September 11, that motto has never seemed more relevant as we have been working to prepare ourselves and the people of the United States for the potential threats that lie before us—particularly the use of our own modern technologies against us.

Fortunately, we have already begun to bring our resources to bear on this challenge. Last year, in response to an act of bioterrorism that was directed against this government, both the Senate and the House worked together in a bipartisan fashion to pass the President's Project Bioshield legislation. I am proud to have been a cosponsor, although I was disappointed that it took a year to complete the process. That new law was a very important first step in the effort to protect this country. We are continuing that journey with our work today.

That legislation gave us a critical head start to meeting the challenge posed by the threat of an outbreak of an infectious disease. It established a permanent market for vaccines and therapeutics that are directed to known and foreseeable agents. It encouraged private industry to generate therapeutics for bioterrorism agents that might be used today. It did not attempt to address all of the impediments that block private industry from more actively partnering to protect our homeland from the threat of bioterror agents. It was a good start that showed the way as we prepare to take the next step in this important effort.

With an established mechanism in place to finance the development of bioterror countermeasures, we must now make sure that it is working and that the necessary resources are in place to ensure the success of our efforts. That will require the cooperation and assistance of an active and engaged biotechnology and pharmaceutical industry, acting as our partners in this effort. We have some of the greatest minds in the country and in the world willing to work with us on what is truly a global problem and a threat to us all, no matter where we live. Using their creativity and expertise we can craft solutions to this problem before they are needed. Clearly, that will be the key to formulating an effective and reliable plan of action on this issue.

We appreciate all the witnesses who are here with us today to share with us their knowledge and insights on this potentially devastating problem. They have come from across the country and around the world to tell us what else is needed to deliver therapeutics to health professionals. I appreciate having Dr. Fauci and Dr. Albright with us to update us on the results of our biodefense efforts. We do need their input and involvement to help us coordinate the efforts of the public and private sectors so that we will be able to rise to the challenge and minimize the danger we face.

Again, I thank Chairman Burr for holding this hearing so that we might have a better understanding of this threat and what we must do to address it. I look forward to working with this subcommittee, other members and stakeholders to take the next steps

that are needed to build a strong national biodefense and ensure the safety of our people for generations to come.

Senator BURR. At this time, since I see our first panel is up, let me welcome both of you once again.

Senator ROBERTS. Mr. Chairman.

Senator BURR. The Senator from Kansas.

Senator ROBERTS. I am riding drag in this posse, and I understand that, and that is my role and I am here for sort of a parochial reason, being the chairman of the Intelligence Committee and also a member of the Agriculture Committee and the Armed Services Committee, but I do have a statement and would ask permission that it be put in the record at this point.

Senator BURR. Without objection, so ordered.

[The prepared statement of Senator Roberts follows:]

PREPARED STATEMENT OF SENATOR ROBERTS

I am pleased that we are holding this hearing today to discuss biodefense and the future. I thank the witnesses for their willingness to share their thoughts on what steps need to be taken to adequately prepare our Nation for the threat of a bioterrorist attack. The events of September 11 forever changed the world in which we live. We have all re-evaluated our priorities and the measures of security which we take. We have upped the level of security and surveillance for our government buildings, sports venues, airports, defense facilities, and economic markets. However, the threat of a bioterrorist attack poses a unique challenge to our public health system. A biological attack can unfold gradually over time, unlike a chemical attack or an explosion where the results are immediate. Therefore, our Nation must depend on the preparedeness of our public health infrastructure to respond quickly and appropriately to a bioterrorist attack.

In recent years, Congress has taken steps to alleviate the threat of bioterrorism. Last July, President Bush signed Project Bioshield into law. Project Bioshield is a step in the right direction for protecting our Nation against bioterror threats. It is no surprise that many potential bioterror agents lack available countermeasures. Project Bioshield was designed to encourage drug and biotech companies to work with the National Institutes of Health (NIH) to develop antidotes, vaccines, and other products to treat and protect against a biological, chemical, radiological, or nuclear attack. BioShield has three principal components: relaxes procedures for bioterrorism-related procurement, hiring, and peer review; guarantees a Federal Government market for new countermeasures for inclusion in the Strategic National Stockpile (SNS); and permits emergency use of unapproved countermeasures. While these steps are positive, I do think there is still room for improvement in areas such as vaccine liability, antitrust issues, and tax reforms, and I am pleased this committee is making Bioshield II a top priority.

When considering the next steps for our biodefense, I believe our agriculture economy and sector should receive no less attention. I believe that security for agriculture merits serious concern by not only the agricultural community but our Nation as a whole. The risk to the U.S. food supply and overall economy is real. A close analysis of the agriculture markets shows that the introduction of

a pathogen such as foot-and-mouth (FMD), avian flu, or Karnal Bunt in wheat could be devastating. FMD is highly noxious and if properly placed in a feedlot or hog confinement facility it could quickly reach epidemic proportions.

In 2002, President Bush signed the Public Health Security and Bioterrorism Preparedness and Response Act into law. The measure is intended to bolster our ability to respond effectively to bioterrorist threats and other public health emergencies. Included in this important piece of legislation are provisions to protect the Nation's food supply and enhance agricultural security. Some of the most significant provisions include:

• Continuation of grants to top agriculture universities and researchers across the Nation to develop vaccines, antidotes and plant varieties that can resist such diseases as Foot-and-Mouth Disease, Karnal Bunt or Avian Flu, as well as other diseases that have been cultivated for use in bio-warfare;

• Provides the agriculture system with a new, enhanced level of protection and biosecurity. This system for first-responders utilizes or is capable of utilizing field test devices capable of detecting biological threats to animals and plants and then electronically integrates the devices and the tests on a real-time basis into comprehensive surveillance, incident management and emergency response system;

• Expansion of the Food Safety Inspection Service (FSIS) by enhancing the ability of the service to inspect and ensure the safety and wholesomeness of meat and poultry products at ports of entry.

In his 2006 budget released just yesterday, President Bush recognized the importance of protecting our Nation's food supply. His request includes a total of $596 million for the Departments of Agriculture, Health and Human Services, and Homeland Security to improve our ability to detect and contain intentional and unintentional contamination of America's agriculture and food system. This is a net increase of $144 million above 2005. President Bush is also requesting a $50 million increase for USDA's monitoring and surveillance activities and a $78 million increase for research by USDA, HHS, and DHS, including research into new detection methods. While I realize the focus of this hearing is not on food security, I do look forward to hearing from our witnesses on their thoughts on how to protect and defend our Nation's food supply. Thank you for your time.

Senator BURR. Let me once again welcome the two of you and at this time recognize Dr. Fauci for his opening remarks.

STATEMENTS OF ANTHONY FAUCI, M.D., DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; AND PENROSE C. ALBRIGHT, PH.D., ASSISTANT SECRETARY FOR SCIENCE AND TECHNOLOGY, DEPARTMENT OF HOMELAND SECURITY

Dr. FAUCI. Thank you very much, Mr. Chairman, Senator Kennedy, Senator Enzi, Senator Roberts. Thank you for giving me the opportunity to testify before this committee this morning regarding the biodefense efforts, particularly at the NIH, and how the re-

search endeavor helps push us toward the development of appropriate and necessary countermeasures.

Before I start describing that, let me briefly outline for you within the Department of Health and Human Services the multifaceted components that go into our biodefense efforts including the Centers for Disease Control and Prevention that was just mentioned by Senator Kennedy which is responsible for surveillance and detection as well as training local response teams.

The NIH conducts the basic and clinical research that lead to the development of medical countermeasures. The FDA has an important regulatory role and the Office of Public Health Emergency Preparedness coordinates all of this. A few years ago, the administration and the Congress gave us an enormous responsibility at the NIH with a very dramatic increase in our budget related to biodefense immediately following the September 11, 2001 tragedy, as well as the anthrax attacks, and this is reflected in the supplement for 2002, and then this enormous increase in budget in 2003, which has been maintained up through and including the current fiscal year and beyond.

This responsibility was taken very seriously by us at the NIH because we knew we had to do the best science possible but also we had a commitment to push for the development of countermeasures. In order to fulfil this responsibility, we immediately brought together blue ribbon panels of the experts in the field of both infectious diseases, microbiology and host defenses immunology and put together a strategic plan for our biodefense efforts as well as two research agendas, one for the Category A agents, the major threats that we will be discussing this morning, as well as one for Category B and C, and I am happy to report that we have already come out with two major progress reports, one in August of 2003 and one in June of 2004, delineating not only the progress in real terms vis-a-vis actual accomplishments but also how we are building the infrastructure for the future years.

If one looks at the plan, it can be divided into a number of components. First and foremost was the necessity to build both the physical and the intellectual infrastructure necessary to perform these tasks over the next few years, and I will mention this briefly in a moment. When I say physical infrastructure, I mean the containment facilities necessary to do the research.

All of this is founded very strongly in basic research, and this is a very important issue, because if we are going to do it, we need to do it right, and good basic research at the point of developing understanding of the pathogenesis of the microbes will be not only important for developing countermeasures in biodefense, but also will be extremely important in extrapolating this to other health issues that might have nothing at all to do with biodefense such as naturally emerging and reemerging infectious diseases and some cancer therapy or what have you.

This ultimately gets translated into the countermeasures as we call them, namely, therapeutics, vaccines and diagnostics.

This is a map of the United States which delineates the various components of the infrastructure that I am talking about. This has rapidly been put in place. Some of these are already being built.

Others, the plans are in place and others we are having planning for the future development of these.

First and foremost among these, we have the Regional Centers of Excellence in Biodefense and Emerging Infectious Diseases—those that are shown in the stars. This is the intellectual capital that is distributed throughout the country, generally associated with Regional Biosafety Labs, or BSL3s, of which there are 9 throughout the country, and most recently, the BSL4s, one in Boston and one in the University of Texas at Galveston Medical Center.

We also have new facilities at the NIH, both on the campus as well as in Fort Detrick and in our Rocky Mountain laboratories in Missoula and Hamilton, Montana.

Getting back to the issue of basic research, I just want to reiterate to you the importance of understanding, for example, the sequencing of the microbes that might be associated with bioterror. We successfully have sequences for virtually every microbe that we consider to be a major threat. This is extremely important when we target vaccines and therapies.

We have developed animal models, but we have also looked at, and again, this gets to the extrapolation to other diseases, host defense mechanisms such as the body's ability to be able to fight against microbes including microbes of bioterror, but also a natural extrapolation to emerging and reemerging infections such as influenza, which we have a threat now as you know of an H5N1 bird flu that we are considerably concerned about.

Let me very briefly just summarize some of the key achievements already. I came before some members of this committee in other hearings regarding smallpox last year and the year before. When we had the events in September of 2001, we had about 15 million doses of smallpox for the 288 million people in this country. We now successfully have over 300 million doses. We have doses for everyone in this country including helping our allies if in fact they need it.

We are not stopping there because we are going to the next generation of a safer smallpox vaccine, the modified vaccinia Ankara, which again is being very rapidly accelerated by the Bioshield that was just mentioned by you and by Senator Kennedy. We are developing antiviral drugs such as an oral drug against a microbe that was originally associated with HIV, cytomegalovirus, and we find that it now has activity against smallpox.

In the anthrax, I think this is the first—it is the first—of the elements of the translation in real terms of Bioshield that was just signed in July of 2004, and that was the procurement of the recombinant protective antigen on the Project Bioshield. We also have the development of novel antitoxins and monoclonal antibodies. We also have a number of other components such as Ebola, influenza and botulism toxin.

Now, Project Bioshield, as you know, is the component that gives us authorities to accelerate. We have emergency approval authority for the FDA, and we also have a set-aside amount of money that we would use as incentive for purchase. The normal paradigm at the NIH is to just do basic and preclinical research and leave it to

the companies because they have enough incentive to develop a product.

We have now had to emphasize the push of that mechanism, namely doing the basic research that pushes through early and advanced development. Project Bioshield provides the pull or the incentive for the companies to actually get involved in signing the contacts that Senator Kennedy mentioned in order to develop products.

We need to continue this partnership between industry and academia and the Federal Government in having this push mechanism meet the pull mechanism.

Finally, I just want to emphasize to you something that I mentioned a few times during the discussion, and that is that the investment in physical and intellectual capital that is associated with our biodefense effort goes well beyond preparing us for agents of bioterror. We look at the people we are training; we look at the facilities that are going on; we look at the products that are coming about. Each of these will inevitably have important positive spinoffs particularly in protecting us against naturally occurring infections such as influenza, SARS and others, but also in other areas such as cancer and other components of public health.

I would be happy to answer questions, Mr. Chairman. Thank you for giving me the opportunity to testify.

Senator BURR. Thank you, Dr. Fauci.

[The prepared statement of Dr. Fauci follows:]

PREPARED STATEMENT OF ANTHONY S. FAUCI, M.D.

Mr. Chairman and members of the subcommittee, thank you for the opportunity to speak with you today. I will discuss our national biodefense research program, with particular emphasis on recent progress toward the development of medical countermeasures against a bioterrorist attack. I am particularly honored to appear at the very first hearing of this subcommittee, and I look forward to working with you to continue to improve our biodefense capabilities which are essential to protecting our Nation's health.

The destruction of the World Trade Center, the attack on the Pentagon and the downing of an airliner over Pennsylvania on September 11, 2001, clearly exposed the vulnerability of the United States to brutal acts of terrorism. The anthrax attacks in Florida, New York and Washington that followed only a few weeks later made it very clear that the threat of bioterrorism with pathogens or biological toxins represents a serious threat to our Nation and the world. The Administration and Congress responded forcefully to this threat, and biodefense has become a top national security priority for which funding has increased substantially. The Department of Defense, the Department of Health and Human Services (HHS), the Department of Homeland Security (DHS), the Department of Agriculture (USDA) and other Federal agencies each have been given important roles to play in biodefense preparedness.

The National Institute of Allergy and Infectious Diseases (NIAID), of which I am Director, is a component of the National Institutes of Health (NIH) and the lead agency within HHS for the conduct of research concerning potential agents of bioterrorism that directly affect human health. Three other components of HHS also are charged with major biodefense responsibilities. Among many roles, the Centers for Disease Control and Prevention (CDC) carries out disease surveillance and detection, maintains the Strategic National Stockpile of medicine and medical supplies for use in an emergency, and trains and advises local public health response teams. The Food and Drug Administration (FDA) is responsible for regulatory approval of new biodefense countermeasures. The Office of Public Health Emergency Preparedness (OPHEP) coordinates all HHS biodefense activities. The President's fiscal year 2006 budget proposal calls for $4.2 billion in funding for HHS bioterrorism preparedness activities, an increase of $154 million over fiscal year 2005.

NIH BIODEFENSE RESEARCH

In the wake of the 2001 terrorist attacks, NIH embarked on a systematic strategic planning process by convening the Blue Ribbon Panel on Bioterrorism and Its Implications for Biomedical Research, comprised of distinguished researchers representing academia, private industry, civilian government agencies, and the military. Based on the panel's advice and extensive discussions with other Federal agencies, NIH developed three key documents to guide its biodefense research program; these are the NIAID Strategic Plan for Biodefense Research, the NIAID Research Agenda for Category A Agents (covering agents that pose the gravest threat to human health, such as those that cause smallpox, anthrax, botulism, and plague), and the NIAID Research Agenda for Category B and C Agents (for agents whose biological properties make them more difficult to deploy or less likely to cause widespread harm than Category A agents).

The Strategic Plan provides a blueprint for the construction of three essential pillars of the biodefense research program: *infrastructure* needed to safely conduct research on dangerous pathogens; *basic research* on microbes and host immune defenses, which serves as the foundation for applied research; and targeted, milestone-driven *medical countermeasure development* to create the vaccines, therapeutics and diagnostics that we will need in the event of a bioterror attack. The two Biodefense Research Agenda documents present detailed descriptions of short-term, intermediate, and long-term goals for research on the wide variety of potential bioterrorism threat agents. NIH also conducts research into ways to mitigate harm to civilians from chemical, nuclear, and radiological weapons. Meeting the goals delineated in the research agendas required a significant expansion of NIH programs already in place that study human pathogens and the immune system. To implement the biodefense agendas, Congress increased NIH appropriations for biodefense research from $53 million in fiscal year 2001 to $1.5 billion in fiscal year 2003 and approximately $1.7 billion in fiscal year 2005; the President has requested $1.8 billion for fiscal year 2006.

The Nation's investment in a strengthened, accelerated and expanded biodefense research program has already begun to return substantial dividends in all three aspects of biodefense research outlined in the Strategic Plan, which has been described in two recent progress reports. Some of the funds are devoted to intramural research, which is work carried out in NIH-owned and operated laboratories; most, however, goes to extramural research funded through grants and contracts awarded to researchers throughout the country at academic institutions and in the private sector.

Infrastructure. Perhaps the most tangible signs of the increased priority for biodefense research are the integrated research facilities under construction to safely contain and study pathogens. In terms of intramural facilities, construction is well under way for new biodefense laboratories. NIAID also is supporting the construction of National Biocontainment Laboratories (NBLs) which will include facilities built to Biosafety Level 4 standards and will therefore be capable of safely containing any pathogen. Nine Regional Biocontainment Laboratories (RBLs), with Biosafety Level 3 facilities, also are planned or already under construction. All of these high-level research laboratories will provide the secure facilities needed to carry out the Nation's expanded biodefense research program in a setting of safety for both workers and the surrounding communities. NIAID also has funded eight Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research (RCEs). This nationwide network of multidisciplinary academic centers will conduct wide-ranging research on infectious diseases that could be used in bioterrorism, and will develop diagnostics, therapeutics and vaccines needed for biodefense. These Centers will develop the human infrastructure that biodefense research will require in the years ahead by serving as a training ground for biodefense researchers, and the Centers will partner with State and local public health agencies to help ensure a strong, coordinated response in a time of crisis.

Basic Research. Advances in the field of medicine rest on a foundation of basic research into the fundamental properties and mechanisms of life. In biodefense, these studies include the sequencing and understanding of microbial genes (genomics), how microbes cause disease (pathogenesis), and how the human immune system and pathogens interact (immunology). NIH-funded basic researchers have made significant progress since 2001 in each of these areas. For example, researchers have determined the genetic sequence of at least one strain of every Category A, B, and C pathogen; in many instances multiple strains have been sequenced, allowing researchers to better understand the factors that determine virulence. NIH has established the Pathogen Functional Genomics Resource Center to help researchers apply and analyze the large new database of genome sequence informa-

tion. In pathogenesis, NIH researchers recently determined the three-dimensional structure of anthrax toxin bound tightly to a target cell surface receptor, and thus have gained a detailed snapshot of a crucial step in the pathway that allows anthrax to kill. This work provides important new leads for the development of novel antitoxins that could save lives late in the disease when large amounts of toxin are present and antibiotics alone are no longer sufficient to save the patient. Finally, immunological studies of the human innate immune system, which is comprised of broadly active "first responder" cells and other mechanisms that are the first line of defense against infection, have been moving forward rapidly. These advances suggest new ways to boost innate immune responses and suggest that it will be possible to develop fast-acting countermeasures that mitigate the effects of a broad spectrum of bioterror pathogens or toxins. Manipulation of the innate immune system also could lead to the development of powerful adjuvants that can be used to increase the potency and effectiveness of vaccines.

Medical Countermeasure Development. The new emphasis placed on biodefense as a national priority has led NIH to develop an expanded paradigm with respect to biodefense product development. NIH has always supported research that generates new knowledge about disease and has worked to translate these findings into vaccines, therapeutics, and diagnostics that protect public health. But to develop safe and effective products for biodefense as quickly as possible, we needed to intensify and accelerate this process. Thus, we have sought creative ways to modify NIH's traditional process of research and development to move ahead more rapidly while continuing to preserve the excellence in basic research that is a hallmark of NIH. Working in close collaboration with industry and academia, we have taken a much more pro-active role in moving promising concepts into advanced product development.

The Project BioShield Act of 2004 signed into law last July provides powerful new mechanisms that will expedite the development and deployment of medical countermeasures for bioterrorism. For example, BioShield gives NIH additional flexibility in awarding contracts, cooperative agreements, and grants for research and development for critical medical countermeasures, and streamlines the scientific evaluation of biodefense research proposals. The pharmaceutical industry has proved to be willing and eager to help in the development of biodefense countermeasures, but it needs a reasonable assurance that a market for these products will in fact exist should industry invest the resources necessary to fully develop them. To help provide these incentives, BioShield establishes a secure 10-year funding source for the purchase and stockpiling of new vaccines and drugs for use in an emergency. To put it another way, BioShield has given us new ways to both "push" and "pull" science toward needed countermeasures—basic research provides the push, and new incentives to industry for product development provide the pull. NIH works vigorously with both.

Much has been accomplished. With respect to medical countermeasures against attack with biological agents, we are already in a far stronger position today than we were only a few years ago. For example, in September 2001 we had 15.4 million doses of smallpox vaccine available; today we have more than 300 million doses. We also have a next-generation safer smallpox vaccine called modified vaccinia Ankara (MVA) in clinical testing and others under pre-clinical development. In addition, a new oral form of an antiviral drug cidofovir is in advanced product development for use in the event of a smallpox attack, as well as to treat the rare but serious complications of the classic smallpox vaccine. For anthrax, NIAID has aggressively pursued a new vaccine called rPA; HHS has contracted with VaxGen, Inc. to purchase 75 million doses of rPA under BioShield. This vaccine is produced using modern vaccine manufacturing techniques and may require fewer doses than the currently licensed vaccine. New anthrax therapies that can neutralize the anthrax toxin are being developed, such as monoclonal and polyclonal antibodies. Candidate antibody treatments for the toxin that causes botulism are in development, as is a new vaccine to prevent the disease. Finally, an Ebola vaccine based on a new strategy is in human clinical trials at the NIAID Vaccine Research Center. I expect the coming years to be at least as productive.

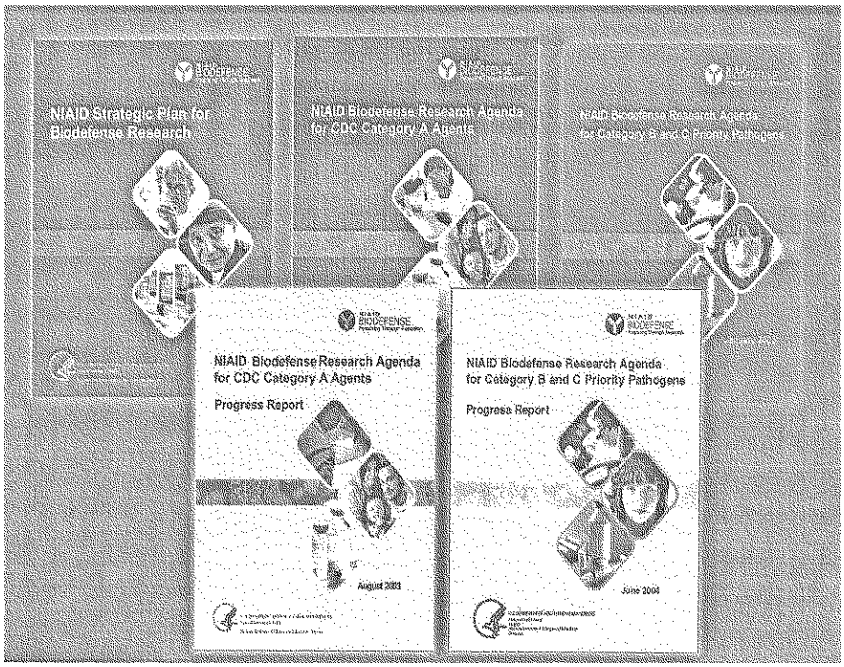
In addition, HHS is pursuing research, development and acquisition of medical countermeasures to address radiological and nuclear threats. These efforts include acquisition programs for a pediatric formulation of potassium iodide under Project BioShield and acquisition of Prussian blue by the Strategic National Stockpile. HHS is also seeking information from industry about capabilities for developing medical countermeasures to treat acute radiation syndrome and exposure to nerve agents.

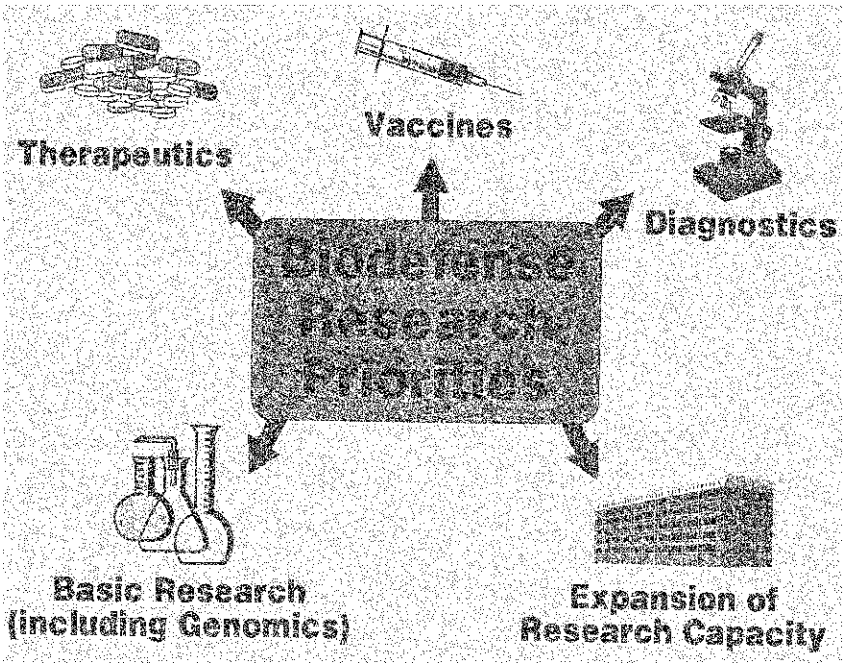
CONCLUSION

I would close with one last point. Infectious diseases have afflicted humanity since its inception, and they will always be with us. The viruses, bacteria, and parasites that cause infectious diseases do not remain static, but continually and dramatically change over time as new pathogens emerge and as familiar ones re-emerge with new properties or in unfamiliar settings. Emerging infections such as HIV, Ebola and SARS and re-emerging infections such as plague and influenza have shaped the course of human history while causing incalculable misery and death. Fortunately, the knowledge and products that will flow from the NIH biodefense research program, including research results, intellectual capital, laboratory resources, and countermeasures in the form of diagnostics, therapeutics, and vaccines, will help us cope with naturally emerging, re-emerging, and deliberately released microbes alike. Recent experience tells us that knowledge developed to understand one pathogen invariably applies to others. When HIV first emerged, for example, antiviral drug development was in its infancy. Now, new technologies have led to the development of more than 20 antiretroviral drugs that can effectively suppress HIV replication and dramatically reduce AIDS morbidity and mortality. These same technologies, and the lessons learned about antiviral drug development, are being applied to the development of new generations of drugs against many viruses, including influenza, SARS, smallpox, and Ebola. Even if we are never confronted with another bioterror attack, the biodefense research and preparations being carried out now will without question prove to be very valuable.

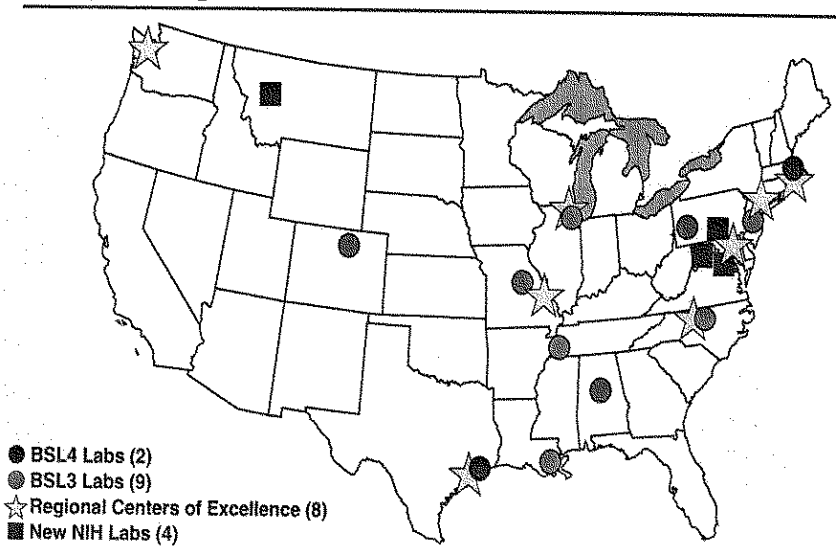
HHS/NIH has a strong mandate from the President and Congress, robust funding, and a detailed and vigorous plan to carry out needed biodefense research. Our long institutional experience with infectious disease research allowed us to seamlessly take on a greatly expanded biodefense role when it became a priority, and I am confident that we are making good progress. Again, Mr. Chairman, I look forward to working with you and the members of the subcommittee to address the challenges of bioterrorism preparedness and its impact on public health.

I am pleased to answer any questions that you may have.

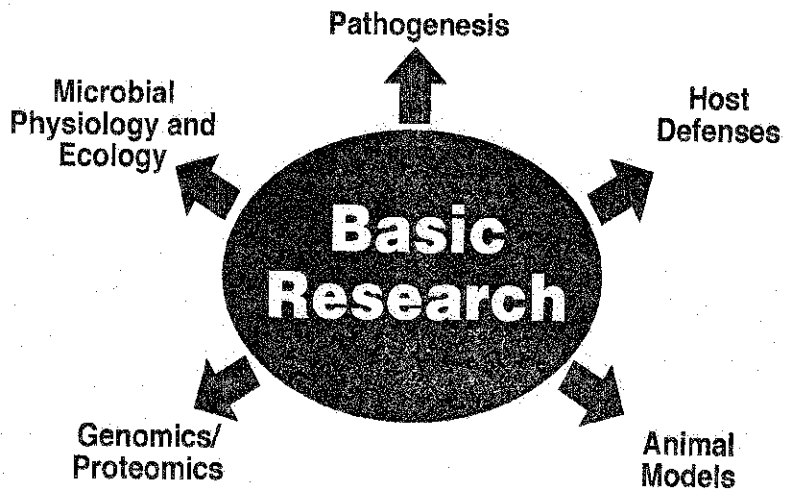




Expansion of Biodefense Research Capacity



Basic Research in Biodefense: Progress and Priorities



Countermeasure Development: Key Achievements

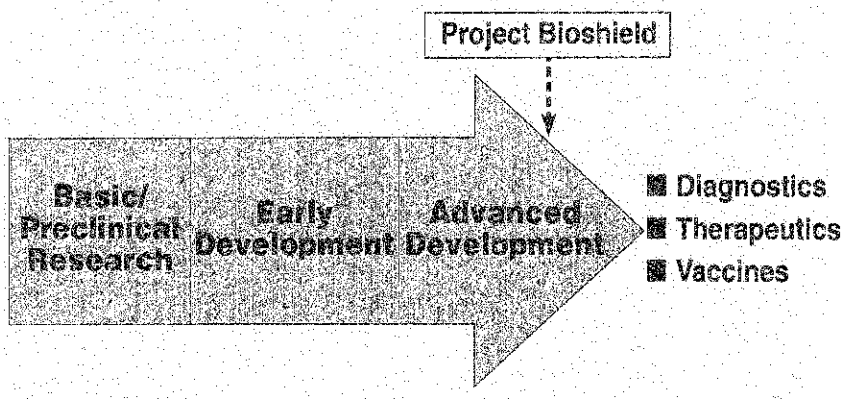
Smallpox

- More than 300 million doses of smallpox vaccine now available
- "Next-generation" vaccine (MVA) in advanced testing
- Antiviral drug development, e.g. oral cidofovir

Anthrax

- New vaccine (rPA) tested and procured under Project Bioshield
- Development of novel antitoxins, e.g. monoclonal/polyclonal antibodies

Countermeasure Development: A Changing Paradigm



Countermeasure Development: Key Achievements (continued)

Ebola

- Vaccine in human trials at NIAID Vaccine Research Center

Botulinum Toxin

- Development of vaccine and monoclonal/polyclonal antibodies

Influenza

- Development of vaccines against potential pandemic strains

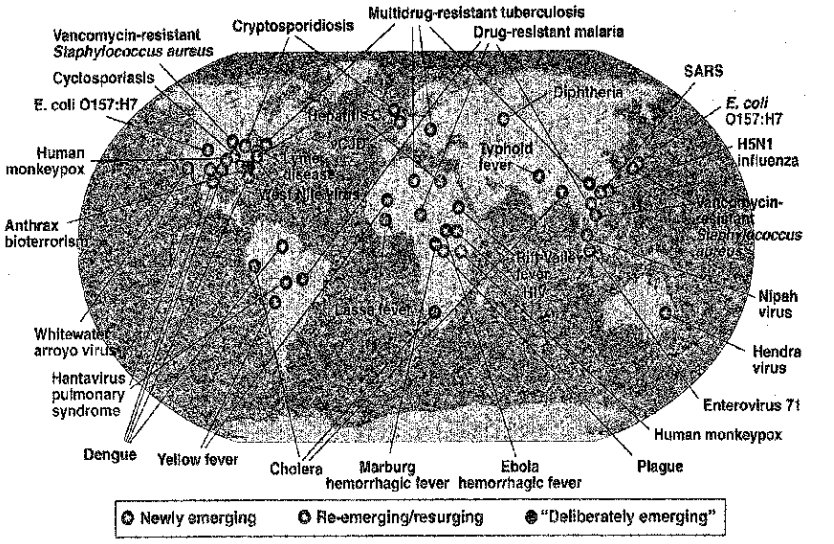
San Francisco Chronicle
NORTHERN CALIFORNIA'S LARGEST NEWSPAPER

FEBRUARY 18, 2002

Bioterror Funds a Boon for Public Health

Experts say research will apply to fighting infectious diseases

Global Examples of Emerging and Re-Emerging Infectious Diseases



Biodefense: Complementary Roles within DHHS

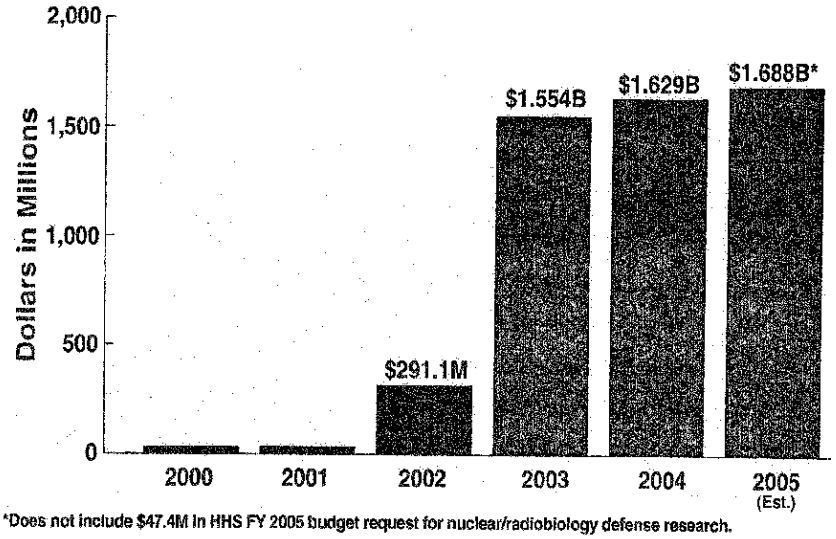
CDC
- Surveillance and Detection
- Train Local Response Teams
- Maintain Vaccine/Antimicrobial Stockpiles

NIH
- Conduct Basic Research
- Develop Medical Interventions
- Develop Research Infrastructure

FDA
- Regulatory Approval
  - Vaccines
  - Therapeutics
  - Diagnostics

OPHEP
- HHS-Wide Coordination of Emergency Preparedness Activities

NIH Biodefense Research Funding, FY 2000-2005



*Does not include $47.4M in HHS FY 2005 budget request for nuclear/radiobiology defense research.

Senator BURR. The chair would recognize Mr. Albright.

Mr. ALBRIGHT. Good morning, Chairman Burr, Senator Kennedy and distinguished members of the subcommittee. I am pleased to appear before you today to discuss the progress the Science and

Technology Directorate of the Department of Homeland Security is making in the Nation's efforts to prevent, protect against, respond to and recover from acts of bioterrorism against the American people.

President Bush has made strengthening the Nation's defense against biological weapons a critical national priority. Although significant progress has been made to protect America, President Bush instructed Federal departments and agencies to review their efforts and find better ways to secure America from bio attacks.

This review resulted in a joint Homeland Security Presidential Directive, HSPD-10, joint along with the National Security Presidential Directive, entitled "Biodefense for the 21st Century," that provided a comprehensive framework for our Nation's biodefense.

This directive builds upon past accomplishments, specific roles and responsibilities and integrates the programs and efforts of various communities—national security, medical, public health, intelligence, diplomatic, agricultural and law enforcement—into a sustained and focused effort against biological weapons threats.

I would also be remiss in not pointing out that a similar activity occurred with regard to the creation of a national effort to protect our agricultural and food industries, and that was embodied in Homeland Security Presidential Directive HSPD-9, and under both HSPD-9 and HSPD-10, the Department of Homeland Security has a role and responsibility in each of the four pillars of the Nation's biodefense programs: threat awareness, prevention and protection, surveillance and detection, and response and recovery. And, in particular, the Science and Technology Directorate has explicit responsibilities in this integrated national effort.

I want to highlight the strategy, planning and accomplishments to date of the Science and Technology Directorate in the area of biodefense and the essential collaborations with key Federal partners including those represented here today.

Before I speak directly to the biodefense efforts of the Science and the Technology Directorate, I want to mention the role of the Department of Homeland Security's Information Analysis and Infrastructure Protection Directorate, and specifically I want to make clear that threat and vulnerability assessments from IAIP are important inputs into the research, development, test and evaluation activities of the Science and Technology Directorate and are critical to the department's decisions regarding the requisite material threat determinations required in order to commit Bioshield funding.

In fiscal year 2004 and 2005, the Science and Technology Directorate deployed the Biowatch Environmental Sensory System to protect our Nation's cities from the threat and ramifications of a bioterrorist attack. We are engaged in creating additional near real-time monitoring. This is the Autonomous Pathogen Detection System, and this is relevant to the protection of critical infrastructure facilities such as major transportation hubs. These were installed, for example, in the Boston subway system during the Democratic National Convention.

We initiated the design of a National Biosurveillance Integration System as part of an interagency process working very closely with Health and Human Services. We conducted preliminary analyses of

four baseline reference cases using a reference scenario approach recommended by HSPD-10 for understanding the requirements of an integrated national biodefense architecture.

We established a Biodefense Knowledge Center, an operational hub for enabling collaboration and communication within the homeland security enterprise and we certified four material threats which, of course, is relevant to the subject of today's hearing, Bioshield.

We established the National Bioforensics Analysis Center to provide a national capability for conducting forensic analysis of evidence from biocrimes and terrorism to attain a biological fingerprint in order to identify perpetrators and determine the origin and method of attack.

In 2006, the department plans to complete the first formal risk assessment that has been required under HSPD-10 and close many of the key remaining experimental gaps in our knowledge of classical biological threat agents. We will complete the deployment of the next generation Biowatch system to the top threat cities while continuing to operate and optimize the already existing Biowatch systems.

We will complete test and evaluation of laboratory prototypes for the third generation of the Biowatch detection system for down select of fieldable prototypes in fiscal year 2007 and continue operation of the National Bioforensic Analysis Center.

We will continue operation of the Plum Island Animal Disease Center and perform essential upgrades to that facility and we will initiate design of the National Bio and Agrodefense Facility. And we will continue to develop bioassays for Foot-and-Mouth disease and other look-alike animal diseases.

The NBACC, the National Biodefense Analysis and Countermeasure Center, is a key component of the national strategy for homeland security and addresses the need for scientific research to better anticipate, prevent and mitigate the consequences of biological attacks.

The NBACC's mission will support two pillars of the blueprint laid out in HSPD-10: threat awareness and surveillance and detection. NBACC is made up of two centers, the Biological Threat Characterization Center and the National Bioforensics Analysis Center I mentioned earlier, to carry out these missions.

We also have a series of university centers that we have established as part of this effort, so within the Science and Technology Directorate, the Homeland Security Centers of Excellence provide independent cutting-edge research within academia for focused homeland security research and development.

We have established centers, and they include a Homeland Security Center for Risk and Economic Analysis, a National Center for Foreign Animal Disease and Zoonotic Defense, and a National Center for Food Protection and Defense. In the next few months, the Science and Technology Directorate expects to establish the Homeland Security Center for Behavioral and Social Aspects of Terrorism and Counterterrorism.

Each center is selected on a competitive basis. Each center has a role of addressing bioterrorism and two are specifically aligned with addressing bioterrorism. Texas A&M University and its part-

ners from the University of Texas Medical Branch, University of California at Davis, and the University of Southern California expect to receive funds over the course of the next 3 years for the study of foreign animal and zoonotic diseases.

The center, which will be known as the National Center for Foreign Animal and Zoonotic Disease Defense, will address potential threats to animal agriculture including Foot-and-Mouth disease, Rift Valley fever, avian influenza and Brucellosis. The Foot-and-Mouth disease research will, of course, be conducted in close collaboration with the department's Plum Island Animal Disease Center.

The Department of Homeland Security expects to provide the University of Minnesota and its partners, Michigan State University, the University of Wisconsin at Madison, North Dakota State University, Georgia Tech and the University of Tennessee, with funds over the course of the next 3 years to establish best practices and attract new researchers to manage and respond to food contamination events both intentional and naturally occurring. The National Center for Food Protection and Defense will address agricultural security issues related to postharvest food protection.

In addition, the Department of Homeland Security and the Environmental Protection Agency are in the process of reviewing proposals for a research Center of Excellence focused on an area of high priority to both agencies, microbial risk assessment for biothreat agents.

The bio-threat agents of interest include bacteria, viruses and biotoxins relating to anthrax, smallpox, botulinum, botulism, plague, viral hemorrhagic fever and tularemia.

Now ensuring that all relevant Federal departments and agencies coordinate in the area of biodefense is critical to protecting the Nation from biological threats. The Science and Technology Directorate has been and continues to be an active participant in relevant interagency activities. A full list of the interagency collaborations has been provided in my statement for the record, and I will just highlight a couple.

As mentioned earlier, HSPD-10 laid out the overall strategy, department and agency roles, as well as specific objectives and calls for periodic reviews to plan, monitor and revise the implementation of our biodefense enterprise.

This was followed by an interagency review that was conducted under the aegis of the NSC and HSC specific to the 2006 to 2010 science and technology needs to support the national biodefense strategy as articulated in HSPD-10.

This and other inputs from a variety of panels such as the Counter Proliferation Technology Coordinating Committee and the National Science and Technology Council's Weapons of Mass Destruction Medical Countermeasures Committee help guide the medical countermeasures procurement activities that are being documented in the National Strategic Plan for Homeland Security Science and Technology as required by the Homeland Security Act of 2002.

The National Science and Technology's Council Weapons of Mass Destruction and Medical Countermeasures Subcommittee, cochaired by myself, provides an interagency forum for discussing

and prioritizing medical countermeasure needs to be pursued under Project Bioshield.

An interagency biosurveillance committee provides a forum for coordinating and integrating the multiple activities in the biosurveillance arena to provide an integrated bio-warning and situational awareness system.

At the next level of coordination there are strong bilateral efforts around key elements of the strategy. Examples of this coordination include strong and frequent collaborations on Bioshield between DHS and HHS, the development of coordinated civilian and military surveillance and detection systems between DHS and DOD, and the development of an execution of a national strategy for agricultural biosecurity and development and assessment of decontamination technologies, the latter with EPA, the former with USDA.

So the science and technology programs conducted within the Department of Homeland Security fully support the National Biodefense Program as stated in the Presidential Directive HSPD-10 and other homeland security presidential directives such as HSPD-9. Moreover, they are conducted in active collaboration with other Federal departments and agencies having a role in meeting this national priority and are focused on reducing the threat of a biological attack against the Nation's population and its agricultural and food critical agricultural infrastructures.

This concludes my prepared statement. With the committee's permission, I would request my formal statement be submitted for the record. Mr. Chairman, Senator Kennedy, and members of the subcommittee, I thank you for the opportunity to testify before you today.

Senator BURR. Thank you very much, both of you, and the chair would ask unanimous consent that the full testimony of all witnesses be included in the record. Without objection, so ordered.

[The prepared statement of Mr. Albright follows:]

PREPARED STATEMENT OF PENROSE C. ALBRIGHT, PH.D.

INTRODUCTION

Good afternoon, Chairman Burr, Senator Kennedy and distinguished members of the subcommittee. I am pleased to appear before you today to discuss the progress the Science and Technology Directorate of the Department of Homeland Security is making in the Nation's efforts to prevent, protect against, respond to, and recover from acts of bioterrorism against the American people.

President Bush has made strengthening the Nation's defenses against biological weapons a critical national priority. Although significant progress has been made to protect America, President Bush instructed Federal departments and agencies to review their efforts and find better ways to secure America from bioattacks.

This review resulted in a Presidential Directive entitled *Biodefense for the 21st Century* that provides a comprehensive framework for our Nation's biodefense. This directive builds upon past accomplishments, defines, specifies roles and responsibilities, and integrates the programs and efforts of various communities: national security, medical, public health, intelligence, diplomatic, agricultural and law enforcement into a sustained and focused effort against biological weapons threats.

The Department of Homeland Security (DHS) and the Science and Technology (S&T) Directorate have explicit responsibilities in this integrated national effort. In particular, I want to highlight the strategy, planning and accomplishments to date of the Science and Technology Directorate in the area of biodefense, and the essential collaborations with key Federal partners, including those represented here today.

BIODEFENSE

Before I speak directly to the biodefense efforts of the S&T Directorate, I want to briefly address the role of the DHS's Information Analysis and Infrastructure Protection Directorate (IAIP), and how their work is linked to the S&T Directorate. IAIP assesses intelligence and information about threats and vulnerabilities from other agencies and takes preventative and protective action. They are partners in the total interagency efforts to obtain, assess and disseminate information regarding potential threats to America from terrorist actions. These threat and vulnerability assessments are inputs into the strategy and research, development, testing and evaluation (RDT&E) activities of the Science and Technology Directorate. For example, agriculture and food are two of the multiple critical infrastructure sectors identified by Homeland Security Presidential Directive 7. As such, they fall within the domain of the IAIP Directorate; they are also within the domain of concern for biological threats and are considered in HSPD-9 and HSPD-10/NSPD-33. In addition, the IAIP Directorate's cooperation with the Science and Technology Directorate is critical to the Department's mission to determine what agents would significantly impact national security if released (Material Threat Determinations).

MISSION AND OBJECTIVES

HSPD-10 outlines four essential pillars of the Nation's biodefense program and provides specific directives to further strengthen the significant gains made in the past 3 years. The four pillars of the program are:

• **Threat Awareness**, which includes biological weapons-related intelligence, vulnerability assessments, and anticipation of future threats. New initiatives will improve our ability to collect, analyze, and disseminate intelligence on biological weapons and their potential users.

• **Prevention and Protection**, which includes interdiction and critical infrastructure protection. New initiatives will improve our ability to detect, interdict, and seize weapons technologies and materials to disrupt the proliferation trade, and to pursue proliferators through strengthened law enforcement cooperation.

• **Surveillance and Detection**, which includes attack warning and attribution. New initiatives will further strengthen the biosurveillance capabilities being put in place in fiscal year 2005.

• **Response and Recovery**, which includes response planning, mass casualty care, risk communication, medical countermeasures, and decontamination. New initiatives will strengthen our ability to provide mass casualty care and to decontaminate the site of an attack.

The Department of Homeland Security has a role and responsibility in each of these four pillars of the national biodefense program. The S&T Directorate has the responsibility to lead the Department's RDT&E activities to support the national biodefense objectives and the Department's mission.

ACCOMPLISHMENTS AND PLANNED ACTIVITIES

In fiscal year 2004 and fiscal year 2005, the Biological Countermeasures portfolio:

• Deployed the BioWatch environmental sensor system to protect our Nation's cities from the threat and ramifications of a bioterrorist attack.

• Engaged in creating additional near real-time monitoring (Autonomous Pathogen Detection System) of critical infrastructure facilities such as major transportation hubs. New infrastructure protection efforts include shorter response time biological agent detection capabilities for BioWatch. This pilot (second generation Bio Watch) is in the process of being deployed in New York City and will join an expansion of the number of collectors in that city.

• Initiated the design of the National Biosurveillance Integration System (NBIS) as part of an interagency process. Recently completed in the first quarter of fiscal year 2005, we will work with the Information Analysis and Infrastructure Protection (IAIP) Directorate to implement this system.

• Conducted preliminary analyses, using the reference scenario approach recommended by Homeland Security Presidential Directive (HSPD)-10 for understanding the requirements of an integrated national biodefense architecture, of four baseline reference cases: a large outdoor release of a non-contagious agent (anthrax); a large indoor release of a contagious agent (smallpox); contamination of a bulk food supply; and two highly virulent agricultural attacks, one on livestock (Foot-and-Mouth Disease) and the other on crops (soy bean rust).

• Established the Biodefense Knowledge Center, an operational hub for enabling collaboration and communication within the homeland security complex. The Biodefense Knowledge Center will meet the operational and planning requirements of

government decision-makers and program planners, the intelligence community, law enforcement officers, public health practitioners, and scientists. Specific capabilities offered to these end-users include knowledge services, modeling and simulation, situational awareness and a pathway to accelerate research and development.

• Certified four "material threats" (anthrax, smallpox, botulinum toxin, and radiological/nuclear); will complete the rest of the Category A bioagents (plague, tularemia) by the end of fiscal year 2005.

• Established the National Bioforensic Analysis Center (NBFAC) to provide a national capability for conducting forensic analyses of evidence from bio-crimes and terrorism to attain a "biological fingerprint" to identify perpetrators and determine the origin and method of attack. The NBFAC was named in HSPD-10 as the lead Federal facility to conduct and facilitate the technical forensic analysis of materials recovered following a biological attack in support of the appropriate lead Federal agency [in most cases the lead Federal agency will be the Federal Bureau of Investigation (FBI)].

In fiscal year 2006, the Biological Countermeasure portfolio plans to:

• Complete the three high-level architectures initiated in fiscal year 2005, identifying key requirements for each major element, a "report card" on the current and projected status in that area and performing detailed design tradeoffs for those areas in which DHS has execution responsibility.

• Complete the first formal risk assessment required under HSPD-10 and close many of the key remaining experimental gaps in our knowledge of the classical biological threat agents. Near-mid, and long-term plans for dealing with engineered agents will be developed, and R&D on addressing the gaps in responding to genetically modified organisms (e.g., antibiotic resistant) initiated.

• Complete the deployment of Generation 2 BioWatch systems to additional cities while continuing to operate and optimize already extant BioWatch systems.

• Complete test and evaluation of laboratory prototypes of the Generation 3 BioWatch detection systems for selection of fieldable prototypes for fiscal year 2007.

• Continue operation of the interim National Bioforensic Analysis Center. International Organization for Standardization (ISO) certification is expected to have been achieved, giving the analyses conducted additional credibility and authenticity in both the national and international community and courts of law. R&D will continue on the physical and chemical signatures of the "matrix" materials associated with biological agents so as to develop methods for understanding tell-tale remnants of enrichment media, culture conditions, metabolites, and dispersion technology.

• Continue operation of the Plum Island Animal Disease Center (PIADC) and essential upgrades to the facility and initiate design of the National Bio and Agrodefense Facility (NBAF). R&D will continue on next generation vaccines and antiviral therapeutics for foot and mouth disease (FMD) and other high priority foreign animal diseases.

• Continue to develop bioassays for FMD and look-alike animal diseases. The initial agricultural forensic capability established in fiscal year 2004 at PIADC will be enhanced and epidemiologic capability added. A High Throughput Diagnostics Demonstration will be initiated to work with regional and State laboratories to demonstrate a capability of analyzing thousands of samples per day in support of response to a suspected case or an outbreak. A FMD table top exercise will be conducted, and development of a coupled epidemiological and economic model for FMD will begin. The end-to-end systems study initiated in fiscal year 2004 for Soybean Rust and FMD will be completed, and system studies will be initiated for highly pathogenic avian influenza.

NATIONAL BIO-DEFENSE ANALYSIS AND COUNTERMEASURES CENTER (NBACC)

The NBACC, a key component of the *National Strategy for Homeland Security*, addresses the need for scientific research to better anticipate, prevent, and mitigate the consequences of biological attacks. The need for the NBACC facility is further defined in HSPD-10, the Nation's blueprint for future biodefense programs. The NBACC's mission will support two pillars of this blueprint—threat awareness and surveillance and detection. The NBACC is made up of two centers, the Biological Threat Characterization Center and the National Bioforensic Analysis Center to carry out these missions. Specifically, NBACC's mission is to:

• Understand current and future biological threats, assess vulnerabilities, and determine potential impacts to guide the research, development, and acquisition of biodefense countermeasures such as detectors, drugs, vaccines and decontamination technologies;

• Provide a national capability for conducting forensic analysis of evidence from bio-crimes and terrorism to attain a "biological fingerprint" to identify perpetrators and determine the origin and method of attack.

In fiscal year 2004, the Department completed the planning and conceptual design of the NBACC facility. Additionally, the Department has been working through the National Environmental Policy Act (NEPA) process during the year, which culminated in the signing of the Record of Decision in January 2005 of the Final Environmental Impact Statement (EIS) for the construction project and subsequent operations. It was decided to delay the award of any contracts for design and construction until further in the EIS process. As the public concerns are analyzed and considered it is anticipated that contracts will be awarded in fiscal year 2005 to initiate design and construction of the NBACC facility.

In fiscal year 2005, the solicitations of contracts for the design and construction of the NBACC facility are expected to be awarded. The design of the NBACC facility will commence in March 2005. Congress appropriated $35 million in obligated funds for award of the construction contract in the fourth quarter of fiscal year 2005. Construction of the facility is planned for completion by the fourth quarter of fiscal year 2008.

UNIVERSITY CENTERS OF EXCELLENCE

The mission of the University Programs is to stimulate, coordinate, leverage and utilize the unique intellectual capital in the academic community to address current and future homeland security challenges, and to educate and inspire the next generation of scientists and engineers dedicated to homeland security.

Within the University Programs in the S&T Directorate, the Homeland Security (HS) Centers of Excellence provide independent, cutting-edge research in academia for focused areas of homeland security Research and Development (R&D). Established centers include: the Homeland Security Center for Risk and Economic Analysis of Terrorism Events, the National Center for Foreign Animal Disease and Zoonotic Defense, and the National Center for Food Protection and Defense. In the next few months, the S&T Directorate expects to establish the Homeland Security Center for Behavioral and Social Aspects of Terrorism and Counter-Terrorism. Each Center is selected on a competitive basis, and each grant is for 3 years. Each Center has a role in addressing bioterrorism and two are specifically aligned with addressing bioterrorism.

DHS awarded funds, over 3 years, to the University of Southern California (USC) and its major partners, University of Wisconsin at Madison, New York University and Structured Decisions Corporation (affiliated with MIT) to establish the Center on Risk and Economic Analysis of Terrorism Events. The mission objectives are to evaluate the risks, costs and consequences of terrorism and to guide economically viable investments in countermeasures. Specifically, the Center will develop risk assessment and economic modeling capabilities that cut across general threats and targets, in application areas such as electrical power, transportation and telecommunications. Additionally, USC and their partners will develop tools for planning responses to emergencies, to minimize the threat to human life and reduce economic impacts of terrorist attacks.

Texas A&M University and its partners from the University of Texas Medical Branch, University of California at Davis, and the University of Southern California expect to receive funds over the course of the next 3 years for the study of foreign animal and zoonotic diseases. The Center, which will be known as the National Center for Foreign Animal and Zoonotic Disease Defense, will work closely with partners in academia, industry and government to address potential threats to animal agriculture including Foot-and-Mouth Disease, Rift Valley fever, Avian influenza and Brucellosis. The Foot-and-Mouth Disease research will be conducted in close collaboration with DHS's Plum Island Animal Disease Center.

The Department of Homeland Security expects to provide the University of Minnesota and its partners, Michigan State University, University of Wisconsin at Madison, North Dakota State University, Georgia Institute of Technology, and the University of Tennessee at Knoxville with funds over the course of the next 3 years to establish best practices and attract new researchers to manage and respond to food contamination events, both intentional and naturally occurring. The University of Minnesota's National Center for Food Protection and Defense, will address agricultural security issues related to post-harvest food protection.

Negotiations began January 10, 2005, for a 3 year grant with the University of Maryland for a fourth Center on Behavioral and Social Research on Terrorism and Counter-Terrorism. We expect its mission objectives to be to provide strategies for intervention of terrorists and terrorist organizations and to embolden the resilience

of U.S. citizens. Major domestic partners include, the University of California at Los Angeles, University of Colorado, Monterey Institute of International Studies, University of Pennsylvania, and the University of South Carolina.

A broad agency announcement was released in mid-January for proposals for a fifth DHS Center of Excellence on the topic of High Consequence Event Preparedness and Response.

In addition to the University Centers of Excellence, the Department of Homeland Security's University Programs and the Environmental Protection Agency's Science to Achieve Results (STAR) Program are reviewing proposals for a research Center of Excellence focused on an area of high priority to both Agencies, Microbial Risk Assessment (MRA) for Category A bio-threat agents.

INTERAGENCY COLLABORATION

Ensuring that all relevant Federal Departments and agencies coordinate in the area of Biodefense is critical to protecting the Nation from biological threats. The previously mentioned HSPD-10, as well as other directives including HSPD-9, Defense of United States Agriculture and Food; HSPD-8, National Preparedness; HSPD-4, National Strategy to Combat Weapons of Mass Destruction; and HSPD-7, Critical Infrastructure Identification, Prioritization, and Protection, identify national objectives and priorities, and departmental and agencies' roles in addressing these national objectives.

The S&T Directorate has been, and continues to be an active participant in these interagency activities as illustrated by our participation in the biodefense program. At the highest level HSPD-10/NSPD-33 laid out the overall strategy, department and agency roles, as well as specific objectives and called for periodic reviews to plan, monitor and revise implementation. This was followed by an interagency review, of specific fiscal year 2006–fiscal year 2010 science and technology needs to support the national biodefense strategy as articulated in HSPD-10.

The National Science and Technology Council's Weapons of Mass Destruction Medical Countermeasures Subcommittee (WMD-MCM), co-chaired by the Assistant Secretary of the S&T Directorate, provides an interagency forum for discussing and prioritizing medical countermeasure needs to be pursued under BioShield. At still the next level of coordination, there are strong bilateral efforts around key elements of the strategy. Examples of this coordination including strong and frequent collaborations on Bioshield (HHS/DHS), the development of coordinated civilian and military surveillance and detection systems (DHS/DOD), the development and execution of a National Strategy for Agricultural Biosecurity (DHS/USDA), and development and assessment of decontamination technologies (DHS/EPA).

In addressing these activities, DHS has a leadership role in several key areas and partners with lead agencies in others. Those areas in which the S&T Directorate provides significant leadership are:

- Providing an overall end-to-end understanding of an integrated biodefense strategy, so as to guide the Secretary and the rest of the Department in its responsibility to coordinate the Nation's efforts to deter, detect, and respond to biological acts of terrorism.
- Providing scientific support to the intelligence community and the IAIP Directorate in prioritizing the bio-threats.
- Developing early warning and detection systems to permit timely response to mitigate the consequence of a biological attack.
- Conducting technical forensics to analyze and interpret materials recovered from an attack to support attribution.
- Operation of the Plum Island Animal Disease Center to support both research and development (R&D) and operational response to foreign animal diseases such as foot and mouth disease.

DHS also supports our partnering departments and agencies with their leads in other key areas of an integrated biodefense: the Department of Health and Human Services (HHS) on medical countermeasures and mass casualty response; the U.S. Department of Agriculture (USDA) on agriculture biosecurity; USDA and HHS on food security and the Environmental Protection Agency (EPA) on decontamination and on water security.

In addition, the Science and Technology Directorate has engaged with other Federal Agencies in the following efforts:

- The S&T Directorate worked with DOS (STAS), USDA, OSTP, NSF to create and support the U.S.-Japan Safe and Secure Society forum.
- The Directorate and DOS (OES) jointly created and negotiated the U.S.-U.K. S&T Memorandum of Agreement (MOA). The resulting MOA supports collaboration

on Homeland Security research, development, testing, and evaluation between the U.S. and the U.K.

• Currently leads a partnership with CDC, EPA, and FBI on the deployment of BioWatch, a bioaerosol detection system deployed to many of this Nation's cities.

• Funds BioNet—DTRA executed pilot program to integrate civilian and military domestic biodetection and consequence management, using San Diego as a pilot city.

• Leading an interagency effort with HHS, DOD, and USPS to develop a National Integrated Biomonitoring System, part of HSPD-10 responsibility.

• Primary participant in the establishment of the National Interagency Biodefense Campus being developed at Ft. Detrick.

• The National Bioforensics Analysis Center (NBFAC) is a joint Science and Technology Directorate-FBI program.

• In a joint effort with USDA, have developed an integrated national agrodefense strategy, with especial emphasis on foreign animal disease. The Directorate and USDA also conduct joint research and development programs at the Plum Island Animal Disease Center.

PRESIDENTIAL INITIATIVES

Three Presidential Initiatives address the needs of an integrated biodefense strategy and DHS plays a key role in each one. These three initiatives are:

BioShield: Signed into law July 21, 2004, BioShield is a program coordinated by the Secretary for Homeland Security and the Secretary for Health and Human Services that provides $5.6 billion over 10 years for the purchase and development of countermeasures to WMD. DHS's S&T Directorate plays a significant role in this in determining which agents constitute "material threats" and in developing scenarios that inform decisions on the quantity of countermeasures required. We have certified four "material threats" (anthrax, smallpox, botulinum toxin and radiological/nuclear and the rest of the Category A bioagents should be completed by fiscal year 2006.

Biosurveillance Initiative: A program that seeks to enhance systems that monitor the Nation's health (human, animal and plant) and its environment (air, food, water) and to integrate these with intelligence data to provide early detection of an attack and the situational understanding needed to guide an effective response. The S&T Directorate plays a major role in the Biosurveillance Initiative in operating its 1st Generation BioWatch System, in deploying a 2nd Generation system and significantly expanding the number of collectors in the highest threat cities and at key facilities (e.g. transportation systems), and in continuing to develop advanced detection systems to further increase the capabilities. We are also designing the information system that will be used to integrate health and environmental monitoring information from the sector specific agencies with intelligence data from the IAIP Directorate. Implementation of this system will actually be initiated by the IAIP Directorate in fiscal year 2005, but the S&T Directorate will continue to supply subject matter expertise in biological threat and defense.

Food and Agricultural Initiative: Seeks to enhance the security of our agricultural and food infrastructures. DHS activities in this area are led by the IAIP Directorate—but the S&T Directorate brings significant contributions in end-to-end studies of key agricultural and food threats, through the development of advanced diagnostics, and through R&D conducted jointly with USDA at the Plum Island Animal Disease Center.

CONCLUSION

The Science and Technology Directorate's programs conducted within the Department of Homeland Security fully support the national biodefense program as stated in the presidential directive *Biodefense for the 21st Century*, and other Homeland Security Presidential Directives. Moreover, they are conducted in an active collaboration with other Federal departments and agencies having a role in meeting this national priority, and are focused on reducing the threat of a biological attack against this Nation's population and its agriculture and food critical agricultural infrastructures, and supports a science-based forensics and attribution capability.

This concludes my prepared statement. With the committee's permission, I request my formal statement be submitted for the record. Mr. Chairman, Senator Kennedy, and members of the subcommittee, I thank you for the opportunity to appear before you and I will be happy to answer any questions that you may have.

Senator BURR. The chair at this time would recognize the full committee chairman for the purposes of questions.

Senator Enzi.

The CHAIRMAN. Thank you, Mr. Chairman. Dr. Fauci, in Dr. Painter's and Dr. Epstein's written testimony, the NIH research tool guidelines are identified as impediments to developing anti-infective agents. Do you share the concern that these tool guidelines are applied to research with anti-infective agents?

Dr. FAUCI. I am not sure exactly what they are referring to, Senator.

The CHAIRMAN. I think they are referring to the patenting of the broadly applicable research tools such as cell lines and animal models and things like that.

Dr. FAUCI. The patenting components are impediments. This is a very complicated issue, Mr. Chairman, because patents are, as you know, very important incentives for companies and groups to get involved in the development of the countermeasures that we need. One of the problems with it is that when there is a patent and the company is involved and has the patent but does not pursue it, it makes it difficult for other companies to get involved in that issue, if that is what they are referring to.

This is not an NIH issue. This is a Federal Technology Transfer Act issue. So I am not exactly sure what the referral is to an NIH impediment, but we tried to remove most impediments to the kinds of goals that we are trying to set, so I would be happy to discuss and debate that with the person at a different time. Since he is not here, I cannot do that, or he is here, but he is not at the table.

The CHAIRMAN. Sometimes the formats of the hearings make it difficult to cover all the things.

Dr. FAUCI. Yes.

The CHAIRMAN. But we will give you another opportunity after we get more detail on how that works.

Dr. FAUCI. Thank you.

The CHAIRMAN. In this hearing, we are trying to see what some of the potential impediments are and what suggestions there are for overcoming them, and then the committee will be determining whether those are reasonable or not at a later time.

In your written testimony—this will be a little more fair—in your written testimony, you note the important benefits that flow from biodefense research to research on infectious diseases. Current law provides that if any product has a substantial use for a bioterrorism application, a dual use, then the provisions of Project Bioshield would generally not apply.

So if a product for bioterrorism would also help say for AIDS or malaria, Bioshield would not apply. Others have suggested that dual use is a good thing. We want medicines for all the infectious diseases, not just bioterror. So as a medical doctor and the head of the infectious disease at NIH, would you speak to the desirability of applying the Bioshield provisions more broadly?

Dr. FAUCI. In the original discussions of Bioshield, Senator, I was and we were in favor of an extension beyond just the agents themselves that are considered agents of bioterror. As the legislation finally got to its form of being signed, that did not get into the bill.

I think that is something for serious consideration. What I was referring to that I believe is even more important in my statement about the connection between what we do to develop agents that are countermeasures against microbes of bioterror, and how that

impacts on others, is the actual fundamental science that goes into it, the people you train, not necessarily the end product, but the process that brings you up to and including the development of a particular agent, be it a vaccine or what have you, is going to keep us in very good stead when we face a naturally emerging microbe.

We have already seen that with the SARS issue that we faced a year and a half ago as well as what we are going through now with our preparedness for pandemic flu, case in point, the H5N1 avian flu in Asia. So the training of individuals, the infrastructure that was set up, the ability to deal with microbes, sequence them, do the cloning, do the targeted development of countermeasures, has been given a giant shot in the arm by what we are doing with bioterrorism.

I was referring much more to that than to necessarily having a product in the stockpile that goes beyond something that is used as bioterror.

The CHAIRMAN. Thank you. Quick question for Dr. Albright. In your testimony you mentioned that there are four material threats. With regard to those threats, as for now, do we have vaccines, diagnostics or therapeutics for each of those, or how many and what do you think we will have in 12 months or 5 years?

Mr. ALBRIGHT. The four material threats that we certified as part of our responsibilities under Bioshield were smallpox, anthrax, botulinum, and radiological and nuclear issues threats.

For each of those we have certainly a certain amount of arrows in our quiver. I mean obviously we have an extant smallpox vaccine. We have treatment available for botulinum in limited quantities. We have countermeasures for those people who are exposed to radioactive debris, that sort of thing. I think what this is intended to do is not just to promote new capabilities—Dr. Fauci mentioned earlier the MVA smallpox vaccine—that is certainly one of the motivators behind that material threat determination—but also the need to procure significant quantities of these materials.

For example, the amount of botulinum antitoxin that we have in the stockpile or we have distributed, more importantly, to hospitals is probably not sufficient in order to deal with a mass attack or the kinds of attacks that we actually think about.

So the point behind this is to be able to procure sufficient quantities to, in fact, be better prepared for those threats.

The CHAIRMAN. Thank you. My time has expired. I will submit some written questions.

Senator BURR. Thank you, chairman.

Senator Kennedy.

Senator KENNEDY. Thank you. Just to follow up with Senator Enzi, which I think is an excellent point, I think it is useful to have as explicit as possible how you can improve the process and give guidance to the private sector in terms of these other areas as well. I think I have heard that issue raised with some companies, and I think it is useful just following up with what my chairman has said.

I am going to try in a limited time to cover a number of points. I am a strong believer, as Mr. Fauci knows and others—that this is the time of the life sciences. The Congress has understood it. We

are seeing all kinds of possibilities out there. I am a great believer in it.

There are enormous possibilities as well in this whole area of biodefense, but we have seen this dramatic reduction in terms of research, a significant reduction if you factor in the cost of living. We have 3.2 percent inflator, and we are getting .4 percent in terms of inflater. So that is going to affect what you are doing in the research area at the NIH.

If you look over the graph here in terms of the preventive health service and the health service grants, they were $132 million, 2004; $131 million, 2005; zero in 2006. These preventative health service block grants, go to local communities, help local communities in terms of detection and planning, zeroed out—zeroed out.

You talk about the various facilities. We have the chart about your various facilities that you had up there. You have gone from 260 to 270 down to 30. I do not know how you are going to complete your P4, whether it is in Texas or up in Boston, with those kinds of figures. You are going down to $30 million when the costs are up there in Boston are $140 million, $130 million to complete that facility.

So I do not know what these—the presentation is enormously impressive, and I have enormous respect for both of you and money is not everything. But if we are talking about national security, and we are talking about homeland security, and we are talking about biodefense industry, you cannot do it on the cheap on this. And this is a matter, I think, of real concern when we see the cuts in areas which have been-targeted in terms of the homeland security.

Let me ask you, Dr. Fauci, there was concern up in my city of Boston about the biosafety of that lab Level 4. I think you are familiar with the tularemia problem that we have up there and the issues in terms of safety for the Level 4 category is a concern. Safety has always been the number one issue in terms of both the NIH, in terms of the development of the P3 and the P4 facilities. I know that. I know it is for the mayor. I know it is for Boston University.

Could you just very, very briefly indicate to us the kinds of safety and security that you all insist on in terms of moving ahead? Give some assurance to the people in these local communities that safety is first and foremost on your agenda. I have limited time so I am going to try and get one more area.

Dr. FAUCI. It is a very relevant question, Senator, and it is really quite safe. I will forward to your staff electronically a list of at least 9 or 10 of the issues, but let me just mention 1 or 2 of them because we are constrained on time.

First of all, there are extraordinary precautions about limited access, things that go so far as thumbprints, retinal scans, special IDs. The BSL4 that is being built at BU has the classic CDC-government approved specifications such as filtering of all air that goes in and out, double door access, interlocked, so that both cannot be opened. All liquids that go in there are drained into what we call a cook tank where it is subjected to high temperatures before it is released.

All solid waste is autoclaved. Safety cabinets, personnel precautions such as showers and showering down of clothing, disposal

of clothing. It is extraordinarily safe. We take the concerns of the community very seriously, but I can say that it is quite safe. There has not historically in this country been a single incident of a harmful event with a community person associated with a BSL4 facility.

Senator KENNEDY. OK. Just two final areas. One is the coordination between NIH, the DHS and DOD on research, if you could comment? There has been some concern about that. Then, finally, just on your new facility that you are building out at NIH, the vaccine facility, what is the capability of that? I mean how could it respond to a crisis, if you could just make brief comments.

Dr. FAUCI. Yes.

Senator KENNEDY. Thank you, Mr. Chairman.

Dr. FAUCI. Will do, Senator. First of all, with regard to how we coordinate between DOD, DHS, we have a coordinating capability that really emanates out of the Office of Homeland Security and the Homeland Security Council at the White House which we all meet frequently, myself and Parney, and others. We exchange information. We exchange our plans, our strategic plans, so there is quite a good degree of coordination that comes actually straight from the Homeland Security Council.

With regard to your question about the building on the NIH campus, that is going to be a BSL3, not a BSL4. It will serve to consolidate the individuals at NIH who are involved in research on biodefense and emerging infectious diseases. So it will be an increased physical capability, but also putting people in one place so that you can have an intellectual exchange that is necessary to get the best out of the science.

Senator KENNEDY. Thank you, Mr. Chairman.

Senator BURR. Thank you, Senator. Senator Roberts.

Senator ROBERTS. Thank you very much, Mr. Chairman. At this point, I would like to submit for the record a summary of the President's Budget as it applies to Homeland Security. I would note that there is a 3.2 percent increase in bioresponse spending in NIH, a .5 increase in regards to NIH overall. I do this only to add in a matrix and agree with the concerns by Senator Kennedy, but I think it is important that we have the total budget figures in here. So I would ask that that be inserted at this point.

Senator BURR. Is there objection? So entered.

[The material presented by Senator Roberts follows:]

HOMELAND SECURITY

The President's 2006 Budget will continue to ensure the security of the Nation's borders, ports, and transportation systems with enhanced screening of goods and people through programs such as the new Screening Coordination and Operations Office; an increase for the United States Visitor and Immigrant Status Indicator Technology (US-VISIT) system; additional radiological and nuclear inspection equipment; and expansion of the Container Security Initiative. The President's 2006 Budget will also enhance enforcement, border, and port security with increases to the Border Patrol; continued execution of the Arizona Border Control Initiative (ABCI); improvements to the Coast Guard; and new, threat-focused State and local assistance grants.

FISCAL YEAR 2006 BUDGET HIGHLIGHTS

• An 8 percent increase in government-wide, non-defense homeland security spending, including fee-funded activities, over 2005.

• An overall increase of $555 million for the Federal Bureau of Investigation, which is 11 percent above 2005 levels, and a 76 percent increase since 2001. Homeland security funding for FBI increases 21 percent in the 2006 Budget, from $1.736 billion in 2005 to $2.099 billion in 2006.

• $3.6 billion for State and local first-responder grants and other assistance. The 2006 Budget proposes to restructure $2.6 billion of this funding so that the Department of Homeland Security (DHS) can target grants for States, urban areas, and infrastructure to fill critical gaps in State and local terrorism prevention and preparedness capabilities, taking into consideration their threats, vulnerabilities, and needs.

• $50 million to fund Citizen Corps, which brings together local leaders, citizen volunteers, and a network of first-responder organizations in local preparation and response efforts.

PROTECTING CRITICAL INFRASTRUCTURE

• $873 million for DHS' Information Analysis and Infrastructure Protection Directorate, which coordinates the Federal Government's efforts to protect the Nation's critical infrastructure, including commercial assets (e.g., stock exchanges), government facilities, dams, nuclear power plants, national monuments and icons, chemical plants, bridges, and tunnels;

• $600 million for the Targeted Infrastructure Protection Program to assist State and local governments in reducing the vulnerability of critical infrastructure, such as chemical facilities, ports, and transit systems.

• $44 million for the Environmental Protection Agency (EPA to fund its Water Sentinel Initiative to help protect the Nation's water supply. Water Sentinel will utilize current technology and develop new technology to produce an operational water monitoring and surveillance system for threat contaminants.

• In total, the President's Budget for 2006 requests $185 million for EPA's homeland security activities, a 73 percent increase over 2005. This includes:

• $19 million in new funds to develop the necessary capabilities for detection and decontamination of threat agents. This investment in decontamination will strengthen the Federal Government through strengthening near-term capabilities and developing improved methods for the future. Additionally, $12 million is dedicated to meeting EPA's responsibility to establish environmental lab support capacity.

• The Budget also maintains resources of $106 million to continue support for investigation and training activities, technical assistance to States, cooperative research, and EPA's national response teams.

DEFENDING AMERICA'S BORDERS, COASTLINES, AND PORTS OF ENTRY

• $6.9 billion for the Coast Guard, an 11.4 percent increase over the comparable 2005 level. This includes:

• $1.9 billion for the Coast Guard's Port, Waterways, and Coastal Security mission, to fund a variety of high-priority Coast Guard initiatives like armed, high-speed boats in ports with liquefied natural gas terminals, further implementation of the Automatic Identification System to track sea-going vessels and enhance Maritime Domain Awareness, new weapons systems for the Coast Guard's helicopter fleet, and implementation of the Common Operating Picture to enable Coast Guard assets to work better together.

• $966 million for the Coast Guard's Deepwater acquisition project, which will fully recapitalize the agency's fleet of major ships and aircraft, while simultaneously implementing a sophisticated new Command, Control, Communications, Computers, Intelligence, Surveillance, and Reconnaissance (C4ISR) system. This is an increase of 33 percent over 2005 levels.

• $37 million for 210 additional Border Patrol agents, $20 million to continue improving the sensor, communication, and video surveillance capabilities along our borders, and $20 million for the acquisition and replacement of aging Border Patrol aircraft.

• An increase of $176 million for the detention and removal of illegal aliens, including:

• $90 million for increased detention beds and additional detention and removal officers;

• $39 million for the detention and repatriation costs of the ABC I, which aims to deter illegal crossings of the desert;

• $8 million to apprehend alien fugitives and $5.4 million to ensure that aliens convicted of crimes in the United States are deported directly from correc-

tional institutions after their time is served, preventing their release into the community;

• $3.5 million for additional attorneys to prosecute immigration cases;

• $5.4 million to expand custody arrangements for non-criminal aliens, particularly asylum seekers, to help ensure their appearance at immigration proceedings.

• A $5.4-million increase for the Container Security Initiative, which pre-screens cargo before it reaches America's shores.

• $178 million in DHS for improved radiological and nuclear screening equipment at our borders.

• An $8.2-million increase for the Customs Trade Partnership Against Terrorism (C-TPAT) to support partnerships with some of the biggest American importers to improve cargo security.

• A $50-million increase for accelerated deployment of US-VISIT at land border ports of entry and for enhanced access for border personnel to immigration, criminal, and terrorist information. With the 2006 Budget, spending on US-VISIT will total over $1.4 billion through 2006.

IMPROVING AVIATION SECURITY

• More than $4.5 billion for TSA aviation-screening operations, a $400-million increase over 2005. Funding will ensure sufficient resources for 45,000 Federal screeners and 10,000 screening devices nationwide;

• A $26-million increase for the Federal Air Marshals program to protect our Nation's airplanes and passengers;

• $110 million to test technical countermeasures against shoulder-fired missiles for safety and reliability.

SAFEGUARDING AGAINST NUCLEAR, BIOLOGICAL, AND CHEMICAL THREATS

• To focus domestic efforts to combat nuclear terrorism, the Department of Homeland Security will stand up the Domestic Nuclear Detection Office (DNDO). DNDO's primary mission will be to strengthen the deployment of the nuclear detectors at home while working to improve the quality of those detectors over time. The office will integrate domestic nuclear detection efforts undertaken by Federal agencies, governments at the State and local level and the private sector, and will be closely linked with international efforts. DNDO will focus and streamline Federal capabilities in areas such as:

• Research: DNDO will oversee a coordinated approach to radiological and nuclear research efforts at DHS, the Department of Health and Human Services (HHS), and the Department of Energy. The Budget provides $262 million, more than twice the amount in 2005, for DHS research and development of advanced-detection devices to minimize the likelihood of a radiological or nuclear device entering the United States.

• Border Monitoring: DNDO will work to ensure optimal deployment of radiological and nuclear screening equipment.

• Grants: DNDO will work with State and local governments on allocating their grants towards the most effective detection equipment and technology.

• $4.2 billion for HHS, a $154 million increase, to address the threat of bioterrorism;

• $107 million, double the funding level in 2005, for DHS research and development into chemical agent countermeasures.

PROTECTING THE NATION'S AGRICULTURE AND FOOD SYSTEM

• The 2006 budgets for the Departments of Agriculture (USDA), HHS, and DHS include a total of $596 million to improve our ability to detect and contain intentional and unintentional contamination of America's agriculture and food system, a net increase of $144 million above the 2005 enacted level.

• $63 million is provided for an interconnected food lab network to increase the size of the network from 21 to 60 labs and improve the rapid exchange of data.

• Early detection of potential threats will be improved through a $50 million increase for USDA's monitoring and surveillance activities and a $78 million increase for research by USDA, HHS, and DHS, including research into new detection methods.

• The Budget includes $59 million to complete construction of USDA's state-of-the-art animal disease research and diagnostic facility located at Ames, Iowa, which will also support the National Animal Health Laboratory Network.

CYBER SECURITY

• The 2006 Budget provides $94 million in funding to the National Science Foundation for research related to cyber security, which is critical to staying ahead of threats to IT infrastructure.

• The Budget also provides $73 million for the National Cyber Security Division within DHS to monitor, respond to, and notify the general public of cyber threats.

• The Budget also provides $10 million in funding for the Cybercorps program, which funds grants for graduate and undergraduate education in cyber security that will strengthen the future of the IT security workforce.

PROMOTING NATIONAL HEALTH SECURITY

• The 2006 Budget provides an additional $153 million for the Strategic National Stockpile to improve the Nation's ability to respond to biological and chemical weapons attacks with life-saving treatments and supplies, including additional antibiotics to treat anthrax, nerve agent treatments, and chemical countermeasures through the Chempack program.

• The Budget for the Stockpile also includes increased funding for the storage and maintenance of next-generation contermeasures, including a new anthrax vaccine purchased through the President's newly enacted Project BioShield.

• Within the 2006 Budget's nearly $29 billion for the National Institutes of Health, the Administration will continue to fund biodefense research and development activities at $1.8 billion. This includes $50 million for chemical countermeasure development and $47 million for radiological and nuclear countermeasure development.

• The Budget proposes nearly $1.3 billion in investments to bolster hospital preparedness and State and local biodefense preparedness. Included in the total for hospital preparedness is $25 million for a targeted, competitive demonstration program to establish a state-of-the-art emergency-care capability in one or more metropolitan areas.

• The Budget also includes $70 million to improve the emergency health care response to a mass casualty event by allowing the Federal Government to purchase and store deployable medical care units, including medical supplies and equipment that can be delivered to an affected area. This funding will also help ensure the availability of health-care providers in response to an emergency.

NATIONAL BIOSURVEILLANCE INITIATIVE

• Last year, the President proposed a new biosurveillance initiative to provide earlier indication that an attack has occurred, and to more accurately determine its nature and scope by monitoring human, animal, and plant health, the food supply, and the environment. The 2006 Budget will build on this progress with a $218-million investment in the gathering and analysis of this information.

Senator ROBERTS. I know that this hearing is not on food security, although it has been mentioned by Dr. Albright, and I thank you, sir, for your perseverance. I thank you both for your leadership and taking the time to come here. I am pleased that with all of the things in the budget that we worry about—and those of us in agriculture do worry about some of the cuts that have been proposed—the President has included a total of $596 million for the Department of Agriculture, Health and Human Services and also Homeland Security to improve our ability to detect and contain intentional and unintentional contamination of America's agriculture and food system—that is a net increase of $144 million over last year—$50 million increase for USDA's monitoring and surveillance activity, $78 million increase for research by the USDA.

Now this is on purpose. Last year, the White House issued the Homeland Security Presidential Directive. Everything has to be an acronym in Washington. So that is HSPD-9, and it deals with the coordination of food and agriculture security. I know there have been some other concerns and primary concerns on the part of the subcommittee.

But this means that the DHS should be the lead agency in this process, and I am aware of the many steps that the Department of Agriculture has taken in this area, so the questions I would have for you, Dr. Albright, and I will just submit them for the record, because we are on a very limited time schedule here, can you tell me what the Department of Homeland Security is doing to really coordinate these efforts? Specifically, how are you working with the Department of Agriculture, Food and Drug Administration, Health and Human Services, and Defense, and intelligence agencies, and I emphasize that because when I ask everybody—and we have an "oh-my-God-hearing" every week—and as chairman of the Intelligence Committee, I said what keeps you up at night?

One of the things, one of the top threats that we have is in regards to our Nation's food supply. The former department head, when he left, Tommy Thompson, and, you know, rode off into the sunset back to Wisconsin or wherever Tommy is, he said that basically our food supply was not safe, and that raised hell all up and down the ag press, and they came to me and they came to Saxby Chambis, and they came to me as chairman of the Intel committee, and said is that right? How are your efforts really coordinated with the National Security Council? And then basically the President's Homeland Security Council? How many DHS staff, HSC staff and other agency staff are working on this issue? How often does the department meet with other agencies to really try to coordinate these efforts?

I notice on your chart, you have CDC, you have NIH and FDA. You do not have USDA. And you do not have the intelligence folks. Now I know that they are included in this, but I asked—and I have gone over to the DHS and these analysts are very young now and they are loaned from other agencies, and I know that the new head of the agency that has just been approved will do what they can—I found one person, one person, that has an aggie background that is worried about agro-terrorism although we call it food security. We do not call it agro-terrorism anymore because it scares people.

Then, in addition, we have the Assistant Secretary, Jim Moseley, who is in Afghanistan, I think, as I speak, for about the fourth time trying to get ahold of Foot-and-Mouth disease and other diseases that could be imported by the Taliban over here to this country. The Department of Agriculture has conducted several war games. Now this is why I am so worried. At one time about 2 or 3 years ago, we had a war game and it was called Crimson Sky, and it was an attack in regards to Foot-and-Mouth disease from Iraq, but it could be from any country, and I served as president. The reason was that Senator Kennedy was out of town. He had important business.

[Laughter.]

And so consequently, what happened to us is that we had an attack by Iraq. There were six States involved. It is a very easy process. You just put a handkerchief underneath the nose of an infected animal over in Afghanistan. You put it in a ziplock bag. You send it to the United States. You drop it in a feedlot, hopefully not in Kansas, also Wyoming, also North Carolina.

[Laughter.]

You can drop it in Massachusetts if you want to.

[Laughter.]

And so I was president. In 6 days, there is the infestation period and then all hell broke lose. And by "break loose," here is what happened. Number 1, our markets collapsed. Number 2, all of our exports stopped. All agricultural export products stopped.

Number 3, everybody in this room and all throughout America realized that their food supply does not come from grocery stores; by golly, it comes from the farm. So they panicked. At every grocery store in America, there was a panic, and so we had really economic chaos. I ordered a livestock stop-order because governors were marshaling their National Guard—when we had National Guard in our States—okay—and so Oklahoma was putting up National Guard in between Texas, which is a natural thing from time to time

[Laughter.]

But, at any rate, no livestock movement.

So I stopped livestock movement and the Department of Commerce said, sir, you cannot do that, and I fired him. That felt very good as president.

[Laughter.]

Then we had to terminate, we had to terminate thousands and thousands and thousands, hundreds and thousands of critters, trying to figure out how on earth to do that. So we called out the National Guard, active duty force, and you had to do it by shooting them. You do not do it by burning them. That is exactly what happened with Great Britain. That is the wrong thing that you had to do.

We had to dig a ditch in Kansas 29 miles long, the size of a football field wide, so it would not leach into the groundwater and we ran out of ammunition, and then we had PETA there to demonstrate.

[Laughter.]

Then we also had TV and it was one hell of a mess, and we lost strains of cattle and the Nation's food supply was harmed for 1, 2, 3 years.

So you can see why I am a little concerned in regards to what is going to happen in regards to agro-terrorism or food security, and I am concerned there is only one person over there at the Department of Homeland Security, and during the Terrorist Threat Information Center briefing they have every week, I know this comes up, and I urge you with all the questions that I have asked, and I have not even given you a chance to respond, please come back and tell me that we are much better coordinated and we are in much better shape. We are in better shape, by the way, I can tell you that, in terms of our Nation's food supply.

That is why I am here, and I think as I look, one of the egregious things that you did, Mr. Chairman, is that you did not put a time limit thing in front of my name.

[Laughter.]

But I can see it over there by Senator Kennedy and also by Senator Murray.

[Laughter.]

So I will cease and desist if you can answer those questions. Thank you for highlighting that. I think it is one hell of a problem.

Mr. ALBRIGHT. Well—

[Laughter.]

Senator ROBERTS. Why don't you just say you agree and we can get on with it.

[Laughter.]

Mr. ALBRIGHT [CONTINUING]. Yes, sir. I agree, sir. And I look forward to answering your questions. I think we can answer most of those, probably not all of them, and actually what I would like to do is I would be more than happy to bring our people that work agricultural issues to come up and brief your staff at their convenience.

Senator ROBERTS. Why don't we have a briefing to my staff which I can share with all of the people here and then we will not take up their valuable time for questions. Senator Reed and Senator Murray are waiting not so patiently.

Mr. ALBRIGHT. Will do.

Senator ROBERTS. OK. Thank you.

[Questions of Senator Roberts follow:]

QUESTIONS OF SENATOR ROBERTS TO PENROSE C. ALBRIGHT, PH.D.

Question 1. Last year the White House issued Homeland Security Presidential Directive HSPD–9, dealing with the coordination of food and agriculture security. HSPD–9 indicates that DHS should be the lead agency in this process. I am aware of many of the steps USDA has taken in this area both prior to and after this announcement. Can you tell me what DHS is doing to coordinate these efforts? Specifically, how are you working with USDA, FDA, HHS, and the defense and intelligence agencies on this front? How are your efforts coordinated with the National Security Council and the president's Homeland Security Council? How many DHS staff, HSC staff, and other agency staff are working on this issue? How often does the department meet with other agencies to coordinate these efforts?

Question 2. The Department of Agriculture has conducted several "war game" scenarios related to agriculture and food security. I participated in one of these known as "Crimson Sky." It dealt with the impact of an intentional introduction of foot-and-mouth disease into the United States. It revealed the truly astounding impact this could have on not just agriculture but the overall economy. Many State governments have also looked at this issue, and USDA has worked to set up rapid diagnostic networks for both plant and animal diseases. Are you aware of the outcomes of this, and similar, activities conducted by USDA. What role would DHS play in such an outbreak, if it were ever to occur? Have you discussed your response plans, if any with other Federal agencies and State governments?

QUESTIONS OF SENATOR ROBERTS TO THE PANEL

Question 3. We have heard much regarding vaccine disease research for potential bioagent threats. This is important research. I'm interested in whether or not you have conducted, or looked into conducting, similar research on vaccines for animal diseases that could be used as bioagents. In addition, how important do you believe such research should be, in light of recent diseaeses such as SARS and avian influenza, that also have the potential to dramatically impact human health?

Question 4. We currently have in place rapid response teams throughout the Nation that could quickly deploy to address acts of terrorism. Are you doing any work to develop similar teams to deal with agriculture and food security issues, and/or are the current teams trained in these areas as well?

Senator BURR. Thank you, Senator Roberts, and I will not make the same mistake twice. I will get a little time thing right in front of you.

[Laughter.]

We are significantly advantaged by having your knowledge of agriculture and your experience on intelligence and let me assure you that the man to my right has assured me that we will not leave agriculture out of our review from the standpoint of this committee.

Senator Murray.

Senator MURRAY. Senator Reed was here ahead of me.

Senator BURR. Senator Reed.

Senator REED. Thank you very much, Mr. Chairman. I am still trying to process the questions. So forgive me. Senator Roberts even looks a little like Johnny Carson from this vantage point.

[Laughter.]

Senator ROBERTS. He is dead, Jack, for God's sake.

[Laughter.]

Senator REED. And I sound like Ed McMahon.

[Laughter.]

Senator ROBERTS. Now, Jack, cut that out.

[Laughter.]

Senator REED. We do this all the time. Thank you, Senator. Dr. Fauci and Dr. Albright, thanks so much for your testimony and for your service. You mentioned that you have spent months devising a strategy to respond to these threats to the United States, and I am curious about the strategy in terms of how it relates to the need for both public and private participation in the process. You talked about building infrastructure. It seems to me that a lot of this investment involves direct Federal expenditures. We will eventually have legislation before us that talks about granting patent waivers and extensions, et cetera.

I frankly do not think we in Congress are working off the same strategy, or at least appreciation of the strategy your agency has developed.

Can you give us an evaluation of what authority you need in terms of incentives to private industry vis-a-vis government programs? One final point—it seems to me that we are buying products that have very little commercial applicability. Unfortunately, this is not something where we can dovetail on an industry that with a little help will do things because they see a commercial benefit. I would appreciate both your comments, gentlemen.

Dr. FAUCI. You are quite correct, Senator Reed. There is an issue with regard to an incentive to develop and produce a product in which there really is very little commercial interest and that was the main motivating force behind the original Bioshield legislation that was signed this past summer by the President.

With regard to the points that I was trying to make is that in all of us there is what we call "a push and a pull mechanism" because if there is an arena of research that unless it is explored, the concept proving for a particular product will not occur. You can very rarely expect industry to make a major investment, which they usually measure in hundreds of millions of dollars to develop something in which there really is no guarantee of a profit margin.

So what we need to do and have been doing, and that is what I was referring to by my comment of the changing paradigm is to push the process much more toward the development so that when industry sees that there is something there, they can then take that risk, and it is a risk for them, to get involved in doing what needs to be done to produce and develop a product that there will be a guaranteed purchase of.

That was the fundamental matrix and component of Bioshield that was passed recently was to have that funding, but we need to

go beyond that. We need to continue to partner with industry. To think that the government is going to be successful in getting necessary countermeasures without close collaboration with industry I think is folly. We have to partner very closely. That is not only in the things that I spoke about, but also in the things that this committee and others in the Congress are trying to do by strengthening the legislation, and I do believe that Bioshield I, as it is referred to, has already been successful in helping us to get to the goal, but we need to go further.

Senator REED. Let me, if I may, raise another issue. It seems to me, and this is oversimplification, is that we are incentivizing private industry, which is important—I agree with you—to collaborate so that ultimately they will sell products to us, the monopoly purchaser, or the monopsony, whatever the right term is. It seems to me that we might be paying on both sides of the transaction. I mean giving them incentives to produce it and then buying it all at the end. It goes to this notion of limited commercial product value.

Dr. FAUCI. You could interpret it that way, but I see it a little bit differently. I see it that if we do not do that, we are not going to have a product. We are just not. Because we have examined the possibility of doing it all ourselves, and that I do not think is a good idea because industry has the expertise and the capability. It is very unique, the industry in this country, which leads the world, so it seems to me that the best approach would be to do what we are saying, even though it could be interpreted as paying out of both ends. It is so important for the national security that I think it is worth doing.

Senator REED. Let me—and I want Dr. Albright to also comment on these issues—but a final question if I could. You have got a strategy. We have passed Bioshield I. Where are the big gaps now from your perceptive looking at your strategy? What elements are missing? And, again, is it appropriated programs that we have to put money towards or is it a gap in this connection with private industry?

Dr. FAUCI. I think these things need to be explored, which is happening with industry in the components of the Congress that have put forth both S. 3 as well as Bioshield II, and that is what it is that the industry really wants? And the only way you could find that is by discussing it with them because we have tried over the years to get—and you cannot do them all together because of the antitrust laws. You got to individually go to each person and say what is it that you would feel would be important to driving you toward getting us to the goal?

Some talk about liability, some talk about patent protection, some talk about others. I think each of these need to be carefully considered as to what the pros and the cons are. But those are the most commonly mentioned gaps that we have right now.

Senator REED. Thank you, Doctor, and Dr. Albright, please.

Mr. ALBRIGHT. I guess I would just want to echo a little what Tony had to say. The whole point behind Bioshield was, in fact, to incentivize industry. That was the purpose behind it. Whether or not that level of incentivization is sufficient I guess remains to be seen. We have just now gone out of the chute with one procure-

ment, the RPA procurement. Whether there are additional needed incentives required in order to get the kind of biodefense countermeasures in place is, I think, an open question.

My view of this is, that what Bioshield has done has been to substantially reduce the risk from the perspective of the pharmaceutical industry with regard to whether or not they should actually be involved. What we are basically telling them is if you license the product, if you get it through licensure, we are going to buy it, and we are going to buy a whole bunch of it. In the RPA case, we are going to buy 25 million courses of it.

Again, whether that works out on sort of a profit business case for them is something that is very complex. In addition to that, as Tony has pointed out, there are other issues which have pervaded the industry for a long time and really have not much to do with biodefense, have to do with patent protections, liability issues and that sort of thing, and I certainly am not qualified to talk much about them except to point out that I do not think they are really biodefense specific issues.

Senator REED. Thank you very much, gentlemen. Thank you, Mr. Chairman.

Senator BURR. Senator Murray.

Senator MURRAY. Thank you, Mr. Chairman, for this hearing. I was listening to Senator Reed talk about the private industry infrastructure and whether it is going to respond. And I cannot help but think, you know, with our latest experience with the flu vaccine just this past year, and wondering since it is the same infrastructure we are relying on to do all this, are we solving the flu vaccine issue? Is that going to come back at us again next year the same way?

Dr. FAUCI. It likely will come back at us somewhat and the general broad plan, Senator, has been to vaccinate more and more people each year. If you look at the history of what has come out of the department, just a few years ago we vaccinated 40 or 50 and then up to 60 and then 83 million last year, and this year now that we are in, we were hoping to go beyond 100 million. We had a big monkey wrench thrown into things, the contamination of the Chiron plant which essentially cut it in half, which put us into a rather untenable position of trying to hold back vaccinations for people who are not in the high risk groups at the same time as we get people who are in the high risk groups vaccinated.

We need to recover from that. That was a setback and the recovery needs to, one, stabilize the market, and it gets to the same industry interaction with government. We have got to get the industry confident that we will be pushing for vaccinating more and more people. We were aiming at 100. We need to go beyond that. That number may be 150, 180 million and what have you.

When industry sees that there is a stable market, they will get much more involved because it is very risky when you are dealing with something which the financial incentives are low, the process of making the vaccine is risky and the market fluctuates. We are trying to stabilize all of those. You can do it by modernizing the process of making the vaccine, by providing stable markets to know that you are going to be recommending vaccines for many others.

So, in many respects, it relates to what we are saying about biodefense. It is one of those things of having to be able to partner in good faith and with good confidence in industry together with the Federal Government.

Senator MURRAY. Thank you. I appreciate that. I know it is not under the jurisdiction of this committee so called, but it is related and I think we need to not lose our sight on that.

I did want to follow up. Senator Kennedy asked you about the facility in Boston and the University of Washington, which does a fantastic job in Seattle, has also been chosen to be a Level 3 facility for NIH and I recognize the importance of that. I think they do a great job, and we are really proud of what they are doing, but there is a lot of concern within the community and I wondered, following up on Senator Kennedy's statement, you can tell us it is safe, but are you working with the communities, with the universities, to help educate the public about it so that they feel more comfortable with that?

Dr. FAUCI. Indeed we are, Senator, and in fact dealing with the community well ahead of time before you start building things is absolutely critical. We have now enormous experience, some of which is traumatic and some of which is very positive, about needing to get the community to understand exactly what you are doing, why you need to do it, and why you need to do it in that site? The people in Seattle at that university I think have done a good job of that.

They have been an example of how you should do it correctly. Others throughout the country, not as well. We need to strengthen the ties between the community because we find almost invariably if they do not understand beforehand what you are trying to do, there will be that natural reflex of suspicion, and that is a natural response. That is not something that should be criticized. It is a natural response. So it is all in open transparent communication.

Senator MURRAY. OK. Very good. I had one question about the Bioshield proposals, and I think it is really important that we look at what worked, what is working, what is not working, before we move forward down the line, and one of the things we did was change the FDA approval process under Bioshield and made a faster approval process, which I think we all agreed needed to be done in order to expedite some of the products that need to be out there to protect all of us.

But I am concerned that we have not placed a lot of focus, both at FDA and NIH, on the longer-term effects of some of these new treatments and vaccines and where we have particularly seen this is a problem for our military personnel who can be ordered to take new experimental treatments without any long-term or postmarket surveillance being required by DOD or NIH or FDA. This is probably a better question for FDA, but I know that you work closely with them, and wanted to ask you about how we are monitoring the long-term effects of this. The Larium with the malaria treatment that military personnel were ordered to take, we are now hearing about high suicide rates and violence associated with that, and according to some of the DOD officials, they are not even sure who received these treatments so we can follow up with them.

I know that FDA has changed the labeling for that treatment, but I am not sure if members of the military, a lot of them who are civilians today, are even aware of that, and I am not even sure if FDA or NIH is looking at these populations once they leave the military.

That is just one example, but I wanted to ask you this morning if you can tell me what steps NIH is taking to direct research to postapproval or postmarket surveillance?

Dr. FAUCI. In general, the research endeavor with regard to a vaccine by NIH does not include late following of individuals in a classic sense. We are doing more of that now in partnership with the FDA in doing studies of follow-up of people who are multiple years down the pike. This is something that generally has not been part of the regimen of the development and ultimate procurement and distribution of vaccines, but you make a very good point. It is clear that there are situations in which there are late effects and the department in general, and the FDA particularly, is clearly looking at that.

Senator MURRAY. OK. Very good. I think we need to really focus on that because when we do expedite the procedures, we want to make sure that any long-term effects that we do not know during the research at the beginning becomes part of what we use collectively. So thank you very much.

Senator BURR. Thank you, Senator. The chair will recognize himself. Dr. Fauci, you alluded very quickly to the problem, the potential problem, that antitrust laws have on our ability to bring a world together and to address. Is there anything that you would like to add to that comment?

Dr. FAUCI. No, Mr. Chairman, the reason I made that comment, and I am not at all an expert in this, and it would be presumptuous for me to make any kind of recommendation, but I can just put it into the context of how that happened. We were trying to get a feel from the industry about what it is that they really would like to see vis-a-vis incentives when we were in the preparatory phase for the original Bioshield legislation.

And it is extraordinary how concerned the legal counsel are from industry to get more than one person on the same phone call or in the same room because of the antitrust, so I had to keep going from person to person alone. It was a very interesting exercise. There is no such a thing as calling a meeting. You cannot have a meeting except that there are lawyers there who tell everybody to keep quiet so I was talking to myself for awhile, and I thought that maybe if we could loosen that up a little I would have been able to get more information.

Senator BURR. Duly noted and it has come up before that that is an area that we may need to look at. It is one that we go into very delicately even in the conversation mode, but I think it is safe to say that most members of both sides of the Hill believe that well intended efforts like Bioshield usually either slow down or do not happen because of a communication breakdown, and clearly that is one of those obstacles that stand in the way that over time may force you to find a way around it rather than take it head on, and we may not enjoy the full fruits of it.

Let me go to the push-pull methodology that you talked about. I think that we all understand the push and I think for the most part the fact that legislation passed, we all understand the need for the pull. I want to take you in between if I can. Talk to me about how robust the entities are to fill that middle slot which is a guarantee to move product.

Dr. FAUCI. That is an issue, Mr. Chairman—I am glad you brought it up—because there is a middle gap there because, in general, traditionally, the way the NIH research structure is set up, we can only push so far into what is called advanced development. When you have the pull mechanism, for example, of our typical Bioshield legislation, which would sign a contract with a company in which they get money only upon delivering of a product, so it is much easier for a large pharmaceutical company to take the risk of doing that advance development and hope to ultimately be able to recoup the money when they get paid for the contract that they sign. We are finding that in some instances some of them cannot take that risk, particularly the smaller biotech companies.

So what the NIH has been faced with is how far are we going to push our dollars into advanced development, and that is risky because that costs a lot of money and that comes out of the basic research pool also. So we are struggling right now with how far we can push into advance development to get the companies confident enough that they know that this will succeed so they can go through the Bioshield mechanism.

Senator BURR. And when in the pull part of that methodology you begin to alter what a company can do with that product, over and above the guaranteed sale to the Federal Government, what effect does that then have on the large pharma companies and their willingness to participate?

Dr. FAUCI. Well, obviously, restrictions on what they can do with that is something that is chilling to them. They feel, at least in my conversations—I am not speaking about any official policy on our part—but they feel that they would like much more flexibility in what they can do with a particular product. For example, a dual use product, a product that could go into the National Strategic Stockpile for biodefense, but they could also use them for something else. There are strict limitations on that.

Senator BURR. Is it safe to say that the Orphan Drug Act happened because we saw the companies were not willing to invest the research dollars because the end-game was so small?

Dr. FAUCI. Right.

Senator BURR. In relation to everything else they could do?

Dr. FAUCI. Yes. The answer is they are related, Mr. Chairman.

Senator BURR. And that is very similar to what we are dealing with here relative to how many might meet that goal of fulfilling the contract at the end?

Dr. FAUCI. That is correct.

Senator BURR. Real quickly, Dr. Albright, you talked about the need to create a biologic footprint or fingerprint—excuse me. For Senator Roberts, that might be a footprint.

[Laughter.]

Senator ROBERTS. Or a hoof print.

Senator BURR. But a bioforensic analysis center. How close are we to that? How realistic is that goal?

Mr. ALBRIGHT. It is operating today. It is actually taking in thousands of samples every month we get from a wide variety of sources. It is done in close coordination with the FBI. The FBI is a partner. They actually have staff up there, and the need for this was actually a direct result of the anthrax attacks in 2001. I mean something as simple as needing a facility where you can store mailboxes that are contaminated and then treat them as evidence and then what we had right after that attack was a relatively ad hoc activity for sequencing the samples, genetically sequencing them, doing more traditional forensics, things like examining how is the thing milled and what other contaminants might be in the sample and that sort of thing.

What we have now done is we have established this National Biological Bioforensic Center up at Fort Detrick, and it is there now. It is operating.

Senator BURR. Clearly we have made significant advances in our ability of the forensic.

Mr. ALBRIGHT. Absolutely.

Senator BURR. We are not as far along as it relates to therapies or antivirals or something that enables us not to have to go through that process.

The chair would recognize Senator Roberts for several questions with answers.

Senator ROBERTS. I would be happy to yield to the distinguished chairman if he has any questions at this point.

The CHAIRMAN. I thank you. I will submit some questions. The ones I have are the accountant type that are so detailed that hardly anybody would be interested in them but me.

[Laughter.]

[Question submitted by Senator Enzi follow:]

QUESTION OF SENATOR ENZI TO PENROSE C. ALBRIGHT, PH.D.

Question 1. In your written testimony you mention national biodefense for agriculture. Specifically you mention Foot-and-Mouth disease and soy bean rust. Could you briefly describe DHS efforts in regard to agrobioterrorism?

Senator ROBERTS. I study those, Mr. Chairman, every time that you have those. Let me just say that, Dr. Fauci, do not worry about talking to yourself. We do that a lot up here. Six of the 19 hijackers in regards to the World Trade Center attack had extensive agriculture training. Some evidence that the crop dusters that were in question back during that time were not for people but for crops. Noting the bioagents that are available in Pakistan and Iran, Russia, more especially Russia, in places like Obolensk and others, that is why I am so concerned about this, not only in terms of people, but agriculture and our Nation's food supply.

We have heard a lot about vaccine disease research for potential bioagent threats, and it is very important. I am interested in whether or not you have conducted or looked into conducting similar research on vaccines for animal diseases that could be used as a bioagent?

Mr. ALBRIGHT. Absolutely. We are, as you know, partnered with USDA up at Plum Island and the Department of Homeland Secu-

rity is very focused on the development of a wide variety of countermeasures that range from development of new vaccines for things like Foot-and-Mouth disease which is probably the highest consequence of all the threats that we are concerned about, including also rapid diagnostics, the ability, for example, to deploy potentially to the field triage systems, that sort of thing.

In the 2006 budget, as a matter of fact, there is substantial additional dollars in the Department of Homeland Security's budget to develop the next generation Foot-and-Mouth disease vaccine. Now this is done in partnership with Agricultural Research Service which tends to do some of the more fundamental research and we tend to be more focused more on the developmental side, kind of filling the gap, in a sense, in the ag side that Dr. Fauci mentioned exists on the public health side of the fence. But, yes, we are absolutely involved in that.

Senator ROBERTS. Well, then there is SARS and avian influenza that make the papers about every other month in terms of we have the sort of terrorist threat of the month, which is unfortunate because it sort of drives TTIC and other matters. But we have currently in place rapid response teams. We used to call them raid teams. That was on the Armed Services Committee. Then we changed that to CST teams and for the life of me I cannot tell you what CST stands for. To get it appropriated, we were going to call it the Ted team or the Bob Team, but there has been a change, so I think probably Terrorism Homeland Advanced Detail, which is THAD, of course. Being the chairman of the Appropriations Committee, I thought they may get funded. But they were to quickly deploy within 4 hours of anybody or any incident to get back to the national folks and say this is what we are dealing with, and with the many, many exercises that we have had, and one of my questions is are you planning exercises, and I hope that you are, this would become absolutely crucial.

Are you doing any work to develop a similar team to deal with agriculture and food security issues or are the current teams trained in this area as well?

Mr. ALBRIGHT. Well, first, a response to the point about exercises, yes, we do exercises all the time.

Senator ROBERTS. Good.

Mr. ALBRIGHT. We actually have a group of people who spend all their time planning exercises and TOPOFF III is coming up, for example.

Senator ROBERTS. You scared the hell out of us with Dark Winter, by the way.

Mr. ALBRIGHT. Right.

Senator ROBERTS. That was a seminal event.

Mr. ALBRIGHT. Yes, well, you know, we have pretty wild imaginations. It is not hard to come up with scenarios that keep you awake at night. With regard to rapid response teams in the agricultural area, that would be something that USDA would be primarily focused on and not the department, and I really do not know the answer to what they have in existence. So what I would like to do is just get back to you with that one.

Senator ROBERTS. OK. I think perhaps in the Intelligence Committee, we ought to have CDC, NIH, FDA, USDA, and we will toss

in a few more, and maybe we could have a good panel discussion about this because in terms of a national threat, Mr. Chairman, I think it is extremely important. Senator Burr has left, as has everybody else, but at any rate I want to thank him for his leadership. I want to thank you for your leadership in having this subcommittee hearing, and I especially want to thank the witnesses. Gentlemen, persevere, because this is going to be a threat and a challenge for us for some time to come, and thank you for the job that you are doing.

The CHAIRMAN. I want to thank the panel for their testimony and their answers and we will be submitting some more questions in writing, if you would be so kind as to get those back to us so we can finish our planning on biodefense.

The CHAIRMAN. Thank you. If the next panel would take their place.

Senator BURR. As our witnesses are moving to the table, let me take an opportunity to reintroduce Gerald Epstein, the Senior Fellow of Science and Security at the Center for Strategic and International Studies, Homeland Security Program; Mr. Gordon Cameron, CEO of Acambis, a biotechnology company with facilities in Massachusetts; Dr. Jon Abramson, the chair of Pediatrics at Wake Forest Baptist Medical Center, and a member of the CDC Advisory Committee on Immunization Practices; and George Painter, the President and CEO of Chimerix in the Research Triangle Park.

Gentlemen, we welcome all of you. We have already made arrangements that your full testimony is to be included as part of the record, and if you have no objections in the order that we go through, I will start to your right and my left and recognize Dr. Painter.

STATEMENTS OF GEORGE PAINTER, PH.D., CEO, CHIMERIX, INC.; JON ABRAMSON, M.D., PROFESSOR AND CHAIR, DEPARTMENT OF PEDIATRICS, WAKE FOREST UNIVERSITY SCHOOL OF MEDICINE, WINSTON-SALEM, NORTH CAROLINA; GERALD L. EPSTEIN, SENIOR FELLOW FOR SCIENCE AND SECURITY, HOMELAND SECURITY PROGRAM, CENTER FOR STRATEGIC AND INTERNATIONAL STUDIES; AND GORDON CAMERON, CEO, ACAMBIS, PLC

Mr. PAINTER. Thank you, Mr. Chairman, and committee. I appreciate the opportunity to be here and speak to you on the current state of biodefense preparedness and the capacity of the biotechnology and pharmaceutical industries to respond to the biodefense needs of the United States.

I appear before you today as the Chief Executive Officer of Chimerix, Inc., an emerging biotechnology company that is in Research Triangle Park, North Carolina. My testimony is based on over 25 years of experience in the biotechnology and pharmaceutical industry. My primary focus and experience is in drug development, taking drugs from the early discovery stage through approval of the regulatory process to commercialization, specifically in the area of antiviral drugs.

From my perspective, there are two primary challenges facing the emerging biodefense industry. First, it is imperative that existing animal models of viral infection be further developed to a level

that will allow drug developers to provide the Food and Drug Administration with the data necessary to ensure the safety and efficacy of these biodefense medicines.

Second, the Department of Health and Human Services must ensure that the Project Bioshield Act of 2004 is implemented in such a way to convince investors in biotechnology such as Chimerix that a successfully developed biodefense countermeasure can be purchased for the Strategic National Stockpile in a predictable and timely manner.

With support in funding by the National Institute of Allergy and Infectious Disease and funding from private venture capital firms, Chimerix has initiated an aggressive program focused on the development of an oral antiviral drug for the prophylaxis and treatment of smallpox. Originally, the primary goal of our effort was to produce a therapeutic alternative to vaccination to provide protection for the up to 50 million Americans who cannot be vaccinated as a result of compromised immune systems.

This population includes people with cancer, people who have undergone organ transplants, pregnant women and small infants, families of people living with common skin disorders such as eczema and atopic dermatitis, and people living with HIV/AIDS.

While this existing gap in our Nation's preparedness alone warrants investment in the development of safe and effective antiviral treatments, last year, straightforward genetic engineering techniques were used to create a model virus related to smallpox that can allude vaccines and produce 100 percent mortality in mice that were already vaccinated. Were these methods successfully applied to the smallpox virus, variola major, the United States would be left defenseless despite the availability of vaccine.

The single-most critical tool in this effort is relevant animal models that can provide data to ensure the efficacy and determine the appropriate human dose of new drugs. It is both impractical and unethical to study the efficacy of a potential treatment for virulent diseases such as smallpox in humans. Therefore, critical efficacy data must be gathered in animal models under the FDA's animal efficacy rule. The data gathered in that rule takes the place of clinical trials, Phase II/Phase II clinical trials that are usually used to justify the approval and registration of a drug.

Simply put, without a good model, Chimerix nor any other company can develop a good antiviral for the treatment of smallpox infection. While a great deal of excellent research has been undertaken by both the Federal Government and the private sector in response to this critical need, current animal models in mice, rabbits, monkeys, using test viruses, mousepox, cowpox, monkeypox, even variola, human smallpox, are currently inadequate to fully support drug development. Thus, further development of treatments for smallpox is essentially stalled.

Existing animal models cannot, for example, address two key issues that have arisen out of discussions between the FDA and Chimerix on the company's smallpox drug candidate.

First, the disease produced in the animals needs to be analogous as possible to the disease that is going to be seen in humans. In current animal models, the rate and degree of appearance of the infection in the blood is dependent on the type and strain of the

pox virus used, the route of infection—is it IV, is it nasal, is it inter-tracheal, is it aerosol—and how much of the virus is used in the infection. We currently do not know which of these test conditions are appropriate in modeling the human disease.

Second, the treatment in animals need to provide the basis for guiding physicians in the treatment or prophylaxis of a person who has the disease. In order to meet this condition, not only must the disease model be correct, but the uptake, distribution and elimination profile of the drug in the animal must be translatable, directly translatable to that in a human.

Resolving these issues is absolutely critical in allowing us to determine what dose of the drugs should be given, how soon before exposure the drug can be given, and have a good prophylactic effect, and how long after the disease has begun to manifest itself that we can treat someone and still be assured of their recovery.

There is no doubt these issues can be resolved with more effort. However, from a practical standpoint, this will require a significantly higher application of resources since animal experiments are both costly and time consuming, key issue being time.

Additionally, this process can be expedited by creating expanded working groups in which people with experience in drug development meet with animal modeling experts and present are appropriate representatives from the CDER branch of the FDA.

On Friday, I returned from a trip to Russia with a delegation led by Congressman Weldon. On my own initiative, I was able to meet with and talk extensively to the leading former Soviet virologist to obtain information and insight into their experience. Given the widely reported experience of the Soviet Union with smallpox long after the eradication of the disease, these scientists many of whom are now quite elderly, possess a great deal of information about the course of the disease. While I have no doubt the United States has already learned a great deal of information from these individuals, their knowledge about the course of the disease could enormously supplement our understanding and help expedite development of animal models to allow drugs such as those being developed by Chimerix to enter the Strategic National Stockpile sooner. I would strongly encourage Congress to consider support of such interactions as part of Project Bioshield.

Recognize that any uncertainty by investors in companies developing countermeasures caused by unpredictable issues and regulatory challenges such as the animal rule have the direct effect of increasing the cost of developing these countermeasures which in turn are passed on to the taxpayer when the drug is purchased for the stockpile.

Of course, there is always the very clear danger that these challenges drive private investment away entirely, thereby threatening the capacity to produce countermeasures at any price. Coupled with the already uncertain environment surrounding the creation of the emerging biodefense industry, the lack of a clear animal rule is potentially crippling to the development of the warm manufacturing base needed for countermeasure development.

I appreciate the opportunity to speak to you today and happy to answer any questions.

Senator BURR. Thank you, Dr. Painter.

[The prepared statement of Mr. Painter follows:]

PREPARED STATEMENT OF GEORGE PAINTER PH.D.

Chairman Burr, Senator Kennedy, and members of the committee, it is an honor for me to testify before you today regarding the current state of biodefense preparedness and the capacity of the biotechnology and pharmaceutical industries to respond to the biodefense needs of the United States.

I appear before you today as the Chief Executive Officer of Chimerix, Inc. Chimerix is an emerging biotechnology company based in Durham, North Carolina. The company was founded in 2002 to harness a technology developed by Dr. Karl Hostetler, professor of medicine at the University of California, San Diego, and is applying this technology to an existing, FDA licensed antiviral medication for AIDS patients in order to make it effective against orthopoxviruses, in particular, smallpox.

My testimony is based on over 25 years of experience in the biotechnology and pharmaceutical industry. During my career, I have worked for both large pharmaceutical companies such as Burroughs Wellcome Co. (now part of GlaxoSmithKline) and small biotechnology companies such as Triangle Pharmaceuticals, also based in North Carolina (now owned by Gilead Sciences). My primary focus and experience is in the development of effective treatments against viruses such as Hepatitis B and HIV, including being the inventor of lamivudine-HBV for the treatment of hepatitis B and being a member of the development team for AZT, perhaps the most widely used HIV treatment in the world.

Let me begin by thanking the committee for its leadership in this critical public health and national security area. The work of this committee's members, including the leadership of Senator Burr while in the House of Representatives and Senator Kennedy with former-Chairman Gregg in the Senate, in the passage of the Project Bioshield Act of 2004 was a credit to each of you. I applaud President Bush for his vision in announcing Project Bioshield in his 2003 State of the Union Address and look forward to working with Senator Gregg and this committee to see passage of S. 3 this year to further strengthen the Nation's biopreparedness.

From my perspective, there are two primary challenges facing the emerging biodefense industry. First, it is imperative that existing animal models of viral infection be further developed to a level that will allow drug developers to provide the Food and Drug Administration (FDA) with the data necessary to ensure the safety and efficacy of needed biodefense medicines. Second, the Department of Health and Human Services (HHS) must ensure that the Project Bioshield Act of 2004 is implemented in a way to convince investors in biotechnology companies such as Chimerix that a successfully developed biodefense countermeasure can be purchased for the Strategic National Stockpile in a timely and predictable manner. Both of the goals are easily achievable.

With support and funding by the National Institute of Allergy and Infectious Disease (NIAID) and funding from private venture capital firms, Chimerix has initiated an aggressive program focused on the development of an oral antiviral drug for the prophylaxis and treatment of one of the most deadly diseases known to man, smallpox. While naturally occurring smallpox was eradicated almost 30 years ago by the World Health Organization's vaccination program, the events of 2001 have made it clear that terrorists can obtain and will use dangerous pathogens to attack our country. Originally, the primary goal of our efforts was to produce a therapeutic alternative to vaccination to provide protection for the up to 50 million Americans who cannot be vaccinated against smallpox as a result of compromised immune systems. This population includes people with cancer, people who have undergone organ transplant, pregnant women and infants, people and the families of people with common skin disorders such as eczema and atopic dermatitis and people living with HIV/AIDS. While this existing gap in our Nation's preparedness alone warrants investment in the development of safe and effective antiviral treatments against deadly smallpox, last year, straightforward genetic engineering techniques were used to create a model virus related to smallpox that can elude vaccines and produce 100 percent mortality in vaccinated mice. Were these methods successfully applied to the smallpox virus, variola major, the United States would be left completely vulnerable to attack despite the availability of smallpox vaccines.

Against this backdrop, Chimerix has worked diligently to pursue the development of a safe and effective smallpox drug and to expedite the drug development process as much as possible. Reaching this goal requires, in essence, that a new, accelerated paradigm for the discovery and development of antiviral drugs be defined. If successfully implemented, this new paradigm could help protect Americans not only

against biological terrorist attacks, but also against emerging infectious diseases such as SARS.

The single most critical tool in this effort is relevant animal models that can provide data to ensure the efficacy and determine the appropriate human dose of these new drugs. It is both impractical and unethical to study the efficacy of a potential treatment for virulent diseases such as smallpox in humans. Therefore, critical efficacy data must be gathered in animal models. Under the FDA's animal efficacy rule, this data is used in place of the standard Phase II and Phase III clinical trials to support registration of the drug. Thus, animal models acceptable to both drug developers and the FDA are absolutely essential to the successful development of biodefense medicines. Simply put, without an appropriate animal model, neither Chimerix nor any other maker of antiviral drugs will be able to develop medicines to treat smallpox infection. While a great deal of excellent research has been undertaken by both the Federal Government and the private sector in response to this critical need, current animal models in mice, rabbits, and monkeys using test viruses such as mousepox, cowpox, vaccinia, monkeypox, and even human smallpox, are inadequate to fully support drug development under the FDA's animal efficacy rule. Thus, further development of treatments for smallpox is stalled.

Existing animal models cannot, for example, address two key issues that have arisen out of discussions between the FDA and Chimerix on the company's smallpox drug candidate. Firstly, the disease produced in animals needs to be as analogous as possible to the disease that would be seen in a human infected with smallpox. In current animal models, the rate and degree of appearance of the infection in the blood is dependent on the type and strain of the poxvirus used, the route of infection and how much virus is used to induce the infection. We currently do not know which test conditions produce the best model of human disease. Secondly, the treatment in animals needs to provide the basis for guiding physicians in the treatment or prophylaxis of human disease. In order to meet this condition not only must the disease model be correct but the uptake, distribution and elimination profile of the drug in the animal must be translatable to that in a human. Resolving these issues is absolutely critical in allowing us to determine what dose of the drug should be given, how soon before exposure the drug can be given to have a prophylactic effect, and how long after the disease has begun to manifest itself that we can treat someone and be assured of their recovery.

There is no doubt these issues can be resolved with more effort. However, from a practical standpoint this will require a significantly higher application of resource since animal experiments are both costly and time consuming. Additionally this process can be expedited by creating expanded working groups in which people with experience in drug development, animal modeling experts and representatives from the FDA CDER branch all participate. Finally, companies that are working to develop biodefense countermeasures and who are consequently gaining first hand experience in the use of the animal efficacy rule must be incentivized to participate in and contribute to these programs despite the fact that the models and their data will be made available to competitors.

On Friday, I returned from a trip to Russia with a delegation led by Congressman Curt Weldon (R-PA). On my own initiative, I was able to meet with and talk extensively to the leading former-Soviet virologists to obtain information and insight into their experience. Given the widely reported experience of the Soviet Union with smallpox long after the eradication of the disease, these scientists, many of whom are quite elderly, possess a great deal of information about the course of the disease. While I have no doubt the United States has already learned a great deal of information from these individuals, their knowledge about the course of the disease could enormously supplement our understanding and help expedite development of animal models to allow drugs such as those being developed by Chimerix to enter the Strategic National Stockpile as quickly as possible. I would strongly encourage Congress to consider support of such interactions as part of Project Bioshield. I look forward to working with FDA and our partners at NIAID, to explore whether the information available from Russian scientists can help expedite development of proper animal models, and thus, the development of safe and effective treatments against smallpox.

The very practical concerns that require companies such as Chimerix to depend upon the animal rule creates enormous challenges in sustaining a private market solution for development and manufacture of medicines such as our smallpox antiviral. Chimerix, like most biotechnology companies, is funded by private equity investors that must be able to analyze and predict a reasonable return on their investment. Thus, the immediate development of animal models that produce data with the most predictive value is critical not only to ensure the safety and efficacy of these drugs to satisfy the FDA, but also to permit a sustainable business model

to allow private entities to continue to participate in the emerging biodefense industry. Without addressing this problem, the United States and, indeed, the world will be left without a safe and effective drug for the treatment of smallpox.

In addition to addressing the animal rule, Project Bioshield must be implemented in a way to allow the investment community the ability to assess and predict with some degree of accuracy the likelihood that a private entity such as Chimerix can generate an adequate return on investment through development of biodefense countermeasures. The recent award of a large contract for a single vaccine technology to a single company to address anthrax has caused some questions to be raised in the investment community about whether the market is viable for companies developing technologies such as Chimerix's that may be used as part of a drug cocktail. Moreover, it is unclear from the recent request for proposals issued by HHS for countermeasures whether there will be enough certainty regarding the number of doses that are to be procured to attract private investment.

Recognize that any uncertainty by investors in companies developing countermeasures caused by unpredictable markets and regulatory challenges such as the animal rule have the direct effect of increasing the cost of developing these countermeasures, which in turn, are passed on to the taxpayer when the drug is purchased for the stockpile. Of course, there is also the very clear danger that these challenges drive private investment away entirely, thereby threatening the capacity to produce countermeasures at any price. Coupled with the already uncertain environment surrounding the creation of the emerging biodefense industry, the lack of a clear animal rule is potentially crippling to the development of the warm manufacturing base for needed countermeasures.

I very much appreciate the opportunity to offer testimony on this very important public health and anti-terrorism issue. Achieving the objectives of the Project Bioshield Act of 2004 and the Protecting America in the War on Terror Act of 2005 recently introduced in the Senate by Senator Gregg as S. 3 are of the utmost importance to ensuring homeland and national security. Again, I applaud your efforts, and the efforts of President Bush and his administration, and look forward to continuing our work with the Department of Defense, HHS and NIH in this critical area.

I am happy to respond to any questions you may have.

Senator BURR. Dr. Abramson.

Dr. ABRAMSON. Good morning, Mr. Chairman and members of the committee. I am Jon Abramson, Physician-in-Chief of Brenner Children's Hospital and Chair of the Department of Pediatrics at Wake Forest University School of Medicine. I am a pediatric infectious disease specialist. I am the immediate past Chair of the Committee on Infectious Diseases of the American Academy of Pediatrics and currently serve on the Advisory Committee on Immunization Practices to the CDC.

I have served on the CDC's anthrax working group and have coauthored AAP policy statements on the impact of bioterrorism on children and the use of smallpox vaccine in children. I have been asked today by Senator Burr to speak to the Bioterrorism Subcommittee regarding the issue of liability and its impact on being able to effectively plan for and minimize the impact of a bioterrorist attack.

The opinions today that I express are my own and do not represent those of Wake Forest University School of Medicine, the Academy of Pediatrics, the CDC or any other organization.

Immunization is one of the greatest public health achievements of the 20th century and has saved millions of lives. Thanks to the widespread use of vaccines, millions of children and adults have avoided terrible diseases that cause great suffering and even death. For example, before immunization, smallpox caused death in approximately 30 percent of those infected and serious morbidity in many other children and adults.

This disease has now been eradicated from the planet, an unprecedented accomplishment made possible due to the introduction of the smallpox vaccination throughout the world.

Polio, a disease that previously paralyzed approximately 350,000 people worldwide annually will be eradicated during the next decade. In the United States immunizations have reduced by more than 95 percent of the vaccine preventable diseases including measles, whooping cough, tetanus, Hemophilus influenza, previously the most common cause of bacterial meningitis in children.

These vaccines have proven to be very cost effective means for preventing these and other serious infectious diseases.

Despite this reduction of disease due to the immunization program, the fragility of the vaccine supply has never been greater, as demonstrated by the recent shortage of multiple vaccines including most recently those that prevent influenza and pneumococcal disease. The reasons for these shortages are multiple and include:

Many of the vaccine manufacturing plants are old and a considerable investment would be needed to update the plants to meet current FDA standards for good manufacturing practices;

Two, the price of older vaccines is relatively low and the profit potential is greater in other therapeutic areas. This relatively low profitability has led to a number of companies discontinuing a production of some or all of their vaccine products.

The risk of a large liability suit recently has increased despite the protection afforded companies and health care providers by the National Vaccine Injury Compensation Program. For example, some attorneys are attempting to bypass the VICP and bring the allegations that vaccine can cause autism directly to the court.

While each of these reasons contributes to the fragility of the vaccine supply, today I will focus my remarks on the impact that liability and compensation concerns have in allowing us to adequately prepare for the widespread public health emergency such as might occur due to emerging infections in nature such as pandemic flu or a bioterrorist attack.

Indeed, the recent experience with smallpox vaccine clearly demonstrated the effect that liability concerns had on implementing a preventable program designed to protect the American public from a smallpox bioterrorist attack. Some of the liability and compensation problems that arose are as follows:

One, biotechnology companies were reluctant to produce a vaccine unless a national liability program was enacted that would hold manufacturers harmless against any lawsuit that arose from those who developed complications or died as a result of the vaccine.

Two, many medical centers struggled with developing a smallpox vaccination program that would allow them to fulfil President Bush's request to immunize groups of health care workers at various hospitals to care for people infected with smallpox.

Even when the President and Congress assumed liability risks for physicians and hospitals, many did not participate in this program. This was due in part to other liability and compensation issues including liability protection offered did not include injury compensation for health care workers, patients, or household contacts who might accidentally be inoculated with the vaccine virus.

The current Vaccine Injury Compensation Program that was created in the 1980s did not afford the liability and compensation protection necessary to implement a mass vaccination program such as might be needed in a bioterrorist attack or pandemic.

In the 108th Congress, Majority Leader Frist introduced a bill, The Improved Vaccine Affordability and Availability Act, that if passed would have strengthened and made several important modifications to the VICP that would significantly help with liability and compensation issues that arise from the routine U.S. vaccination program

However, it was not the intent that the proposed legislation addressed a widespread public health emergency where rapid vaccination of a very large percentage of the population would be needed to maximally protect both the individuals as well as society.

The Project Bioshield Act of 2004 and the Safety Act attempt to deal with some of these liability issues that arose in response to the smallpox vaccine program, but these pieces of legislation do not go far enough.

So what is needed today to be done to minimize the impact of a bioterrorist attack? Congress needs to enact a no fault mechanism that covers not only bioterrorist attack but any widespread public infectious disease outbreak where emergency interventions such as vaccination would be done on a large-scale basis. It should protect vaccine manufacturers and health care providers from lawsuits due to the potential side-effects of the vaccine and compensate children and adults injured directly or indirectly by the vaccines that are recommended to prevent bioterrorism inflicted disease.

While the Vaccine Injury Compensation Program does need to be modernized and strengthened, any program to address immunizations in the face of a widespread outbreak should be a system separate from the VICP and encompass all circumstances where mass emergency immunization would be necessary.

The program needs to have the following components:

One, protection of the vaccine manufacturer against lawsuits should be absolute except in the case of gross negligence. What do I mean by that? For instance, a failure to follow good manufacturing procedures during the production and distribution of the vaccine.

Two, health care workers and medical facilities participating in the immunization program need complete protection against lawsuits unless they violate standard medical procedures when administering the vaccine. For instance, failure to change needles when withdrawing vaccine from a multidose vial.

Three, those who develop a complication due to the vaccine should be reimbursed for their medical costs and lost earnings, but should not receive punitive damages.

Although the liability and compensation issues raised by a widespread public health emergency due to an infectious agent are multiple and complex, the overall goal is simple: the ability to make the necessary vaccines, administer them to a large number of people, and have a public willing to be immunized. Those events must occur in consecutive order to minimize the impact of such an event.

The Federal Government is the only entity in a position to declare that mass vaccination is necessary and prioritize those who would receive the vaccine. As such, the Federal Government is the logical entity to provide the compensation.

Similar liability and compensation issues will occur if experimental drugs are used to treat patients infected with microbial agents. For example, there are currently no FDA approved drugs to treat smallpox although several antiviral agents are under development. In the event of a smallpox bioterrorist attack, one or more of these drugs might need to be used in an attempt to decrease mortality. The liability and compensation issues and recommendations that I have just discussed for vaccines would also apply to antimicrobial agents.

I urge Congress to thoughtfully, yet quickly, address the need to develop a compensation program to deal with the specific issues raised by a bioterrorist attack. It is critical to minimizing the impact of such an attack on the public health. I thank the committee for letting me testify and would be happy to answer any questions.

Senator BURR. Thank you, Dr. Abramson.

[The prepared statement of Dr. Abramson follows:]

PREPARED STATEMENT OF JON ABRAMSON, M.D.

SUMMARY STATEMENT

Immunization is one of the greatest public health achievements of the 20th century and widespread use of vaccines has prevented millions of people from contracting diseases that can cause great suffering and death. Unfortunately, today the risk of a widespread bioterrorist attack is real and the development and use of vaccines is a critical component to minimize the impact of such an attack. The recent experience with smallpox vaccine clearly demonstrated how liability and compensation concerns can have negative impact on our ability to implement a preventive program designed to protect the American public from bioterrorism.

The current national Vaccine Injury Compensation Program (VICP) that was created in the 1980s does not afford the liability and compensation protection necessary to implement a mass vaccination program. Congress needs to enact a "no fault" mechanism that could be modeled after the VICP, but needs to be more comprehensive to allow for mass vaccination. This program needs to have the following components:

(1) Protection of the vaccine manufacturer against lawsuits should be absolute except in the case of gross negligence (e.g., failure to follow good manufacturing procedures during the production and distribution of the vaccine).

(2) Health care workers and medical facilities participating in the immunization program need complete protection against lawsuits unless they violate standard medical procedures when administering the vaccine (e.g., failure to change needles when withdrawing vaccine from a multidose vial).

(3) Those who develop a complication due to the vaccine should be reimbursed for their medical costs and lost earnings, but should not receive punitive damages.

Although the liability and compensation issues raised by a widespread public health emergency due to an infectious agent, including those caused by a bioterrorist attack, are multiple and complex, the overall goal is simple. The ability to make the necessary vaccines, administer them to a large number of people and have a public willing to be immunized are three events that must occur in consecutive order to minimize the impact of this type of event. Similar liability and compensation protection also needs to be extended to those producing and receiving experimental drugs needed to treat an infection.

Good morning, Mr. Chairman and members of the committee, I am Jon Abramson, M.D. Chair, Wake Forest University Physicians, Physician-in-Chief, Brenner Children's Hospital and Weston M. Kelsey Professor and Chair of Pediatrics at Wake Forest University School of Medicine. I am a pediatric infectious disease specialist. I am the immediate past Chair of the Committee on Infectious Dis-

eases of the American Academy of Pediatrics (AAP) and currently serve on the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention (CDC). I have served on the CDC anthrax working group and have coauthored AAP policy statements on the impact of bioterrorism on children and the use of smallpox vaccine in children. I have been asked by Senator Burr to speak to the Bioterrorism Subcommittee regarding the issue of liability and its impact on being able to effectively plan for and minimize the impact of a bioterrorist attack. The opinions I express today are my own and do not represent those of Wake Forest University School of Medicine, the AAP, CDC or any other organization.

Immunization is one of the greatest public health achievements of the 20th century and has saved millions of lives. Thanks to the widespread use of vaccines, millions of children and adults have avoided terrible diseases that can cause great suffering and even death. For example, before immunization, smallpox caused death in approximately 30 percent of those infected and serious morbidity in many other children and adults. This disease has now been eradicated from the planet, an unprecedented accomplishment made possible due to the introduction smallpox vaccination throughout the world. Polio, a disease that previously paralyzed approximately 350,000 people worldwide annually, will likely be eradicated during this decade. In the United States immunizations have reduced by more than 95 percent other vaccine-preventable infectious diseases including measles, whooping cough, tetanus, and *Haemophilus influenzae*, previously the most common cause of bacterial meningitis in children. These vaccines have proven to be a very cost-effective means for preventing these and other serious infectious diseases.

Despite the great reduction of disease due to the immunization program, the fragility of the vaccine supply has never been greater, as demonstrated by recent shortages of multiple vaccines including most recently those that prevent influenza and pneumococcal disease. The reasons for these shortages are multiple and include:

(1) Many of the vaccine manufacturing plants are old, and considerable investment would be needed to update the plants to meet current FDA standards for good manufacturing practices.

(2) The price of older vaccines is relatively low and the profit potential is greater in other therapeutic areas. This relatively low profitability has led to a number of companies discontinuing production of some or all of their vaccine products.

(3) The risk of large liability suits recently has increased despite the protection afforded companies and health care providers by the national Vaccine Injury Compensation Program (VICP). For example, some attorneys are attempting to bypass the VICP and bring the allegation that vaccines can cause autism directly into court.

While each of these reasons contribute to the fragility of the vaccine supply, today I will focus my remarks on the impact that liability and compensation concerns have in allowing us to adequately prepare for a widespread public health emergency such as might occur due to emerging infections in nature (e.g., pandemic influenza) or a bioterrorist attack. Indeed, the recent experience with smallpox vaccine clearly demonstrated the effect that liability concerns had on implementing a preventive program designed to protect the American public from a smallpox bioterrorist attack. Some of the liability and compensations problems that arose are as follow:

(1) Biotechnology companies were reluctant to produce a vaccine unless a national liability program was enacted that would hold manufacturers harmless against any lawsuits that arose from those who developed complications or died as a result of the vaccine.

(2) Many medical centers struggled with developing a smallpox vaccination program that would allow them to fulfill President Bush's request to immunize a group of healthcare workers at various hospitals to care for people infected with smallpox. Even after the President and Congress assumed liability risk for physicians and hospitals, many did not participate in the smallpox immunization program due, at least in part, to liability and compensation issues. This was because the liability protection offered did not include injury compensation for healthcare workers' patients or household contacts who might be accidentally inoculated with the vaccine virus.

The current VICP was created in the 1980s and does not afford the liability and compensation protection necessary to implement a mass vaccination program, such as might occur from a bioterrorist attack or a pandemic. In the 108th Congress, Majority Leader Bill Frist (R-TN) introduced a bill, the Improved Vaccine Affordability and Availability Act (S. 754) that, if passed, would have strengthened and made several important modifications to the VICP that would significantly help with liability and compensation issues that arise from the routine U.S. vaccination program. However, it was not the intent that this proposed legislation address a widespread public health emergency where vaccination of a very large percentage of the population

would be needed to maximally protect both the individual as well the population as a whole.

So what needs to be done to minimize the impact of a bioterrorist attack? Congress needs to enact a "no fault" mechanism that could be modeled after the VICP. It should protect vaccine manufacturers and health care providers from lawsuits due to potential side effects of the vaccine and compensate children and adults injured directly or indirectly by vaccines that are recommended to prevent bioterrorism-inflicted disease. While the VICP does need to be modernized and strengthened, any program to address immunizations given in response to a bioterrorist attack should be a system separate from the VICP. The program needs to have the following components:

(1) Protection of the vaccine manufacturer against lawsuits should be absolute except in the case of gross negligence (e.g., failure to follow good manufacturing procedures during the production and distribution of the vaccine).

(2) Health care workers and medical facilities participating in the immunization program need complete protection against lawsuits unless they violate standard medical procedures when administering the vaccine (e.g., failure to change needles when withdrawing vaccine from a multidose vial).

(3) Those who develop a complication due to the vaccine should be reimbursed for their medical costs and lost earnings, but should not receive punitive damages.

While I have focused my remarks today on the use of vaccines in a bioterrorist attack, many of the same liability and compensation issues would arise during any widespread public health emergency due to an infectious disease such as will occur the next time there is a pandemic influenza season. Although the liability and compensation issues raised by a widespread public health emergency due to an infectious agent are multiple and complex, the overall goal is simple. The ability to make the necessary vaccines, administer them to a large number of people and have a public willing to be immunized are three events that must occur in consecutive order to minimize the impact of this type of event.

Similar liability and compensation issues will occur if experimental drugs are used to treat patients infected with microbial agent. For example, currently there is no FDA-approved drug to treat smallpox, although several antiviral agents are under development. In the event of a smallpox bioterrorist attack, one or more of these drugs might need to be used in an attempt to decrease mortality. The liability and compensation recommendations I have just discussed for vaccines would also apply for antimicrobial agents.

I urge Congress to thoughtfully, yet quickly, address the need to develop a compensation program to deal with the specific issues raised by a bioterrorist attack. It is critical to minimizing the impact of such an attack on the public health.

Senator BURR. Dr. Epstein.

Mr. EPSTEIN. Thank you, Mr. Chairman. Mr. Chairman, I am Gerald Epstein, a Senior Fellow for Science and Security at the Center for Strategic and International Studies. I have been looking at issues of science, technology and security for my entire career which I cannot resist pointing out I began when I worked for this body. I was initially an analyst at the Congressional Office of Technology Assessment, which is a capability that no longer exists today, but I think it is one that you and the rest of the members of this body and the other would find very useful at precisely the kind of question that we are looking at today.

I would like to spend some time this morning discussing some overall aspects of the bioterrorism threat, what these characteristics imply for our ability to counter these threats, some of the high priority actions that we need to take as a result, and then I want to conclude with a few overall cautions that we have to keep in mind as we think our way through.

Clearly, this is not a hearing all about the threat, and the members of this committee are quite familiar with it. But as we know, history is a very poor guide. We have, I know, few areas with as great a gulf between a demonstrated proven capability to do tremendous damage, on the one hand, and a relative paucity of actual examples of significant human casualties on the other.

We know that major State programs almost 50 years ago have demonstrated the capability that the technologies and equipment available can do tremendous damage. We know that in the intervening 5 decades that the technology, materials and expertise from which this ability arises is propagating around the world and sufficiently motivated terrorists can avail themselves of the ability to produce these weapons.

We also know now something we may not have known more than 5 or 10 years ago, that terrorists do exist who want to kill vast numbers of us. So what we do not know is why they have not applied this capability to that desire. There is a whole other debate which I will not go into, but it may be just that these technologies have been unfamiliar to the people who have tried to commit these acts.

Maybe the generation of terrorists we face today have not taken high school biology. Next generation of terrorists will and tomorrow's high school biology classes will be much more potent than what is available in classes today.

So the capabilities that we are worried about are not only around today, but if one looks at how technology is evolving, the dissemination around the world, its availability to people, the endemic nature in which it is building itself into the economy, means that more and more capability is going to be in the hands of more and more people. I think one debate we sometimes get into is not particularly helpful: here is a given level of capability that terrorists have today and this is what they need to do a major biological attack; how close or how far are we? That is an important question if I want to worry about what is my chance of being attacked today.

But the questions in front of this committee involve preparations that will take many years to put in place. We have to look down the road, not what today's threat is going to be, but what the threat is going to be years out when the systems that we are talking about and voting funds for today are put into place. So no matter what that gap may be right now, it is going to be smaller next year and smaller the year after that, and eventually we just have to assume that the capabilities will be available.

So what does this tell us about the nature of the future threat? First of all, it is unpredictable in detail. We know, and I appreciate Senator Roberts' interest in particular—he has a very hard job with the intelligence oversight and the intelligence agencies—the amount of effort one needs, the footprint, as it has been referred to, for producing biological weapons can be very small. Maybe even harder, the natural background of legitimate biotechnology activity all over the world is large and is increasing. So we are looking for a very small signal in a very large background. It is going to be very difficult to find these activities.

Second major aspect is that while our defensive efforts take some time to put into motion, particularly when we are talking about drugs and therapeutics and approval, the activities of those developing weapons can be much more flexible and much more rapid. So these all say that we are not going to be able to rely on intelligence to give us firm details about the problem we are worried about.

We are not going to be able to say these are the lists of bugs we know people are going to work on. These are the ones we know are

the problems. We can say there are some agents that are more serious than others. And those are the ones that we are working on today.

But looking out into the future, we are not going to be able to pick off one by one by one. We have to prepare a broad response and a rapid flexible biodefense capability if for no other reason than the threat we may face in 10 years does not exist today. The groups that are going to be posing that threat may not have formed so we are not going to be able to steer directly our efforts based on hard, firm intelligence. We have to develop broad capabilities.

This then goes directly to the question of some therapeutics, antiinfectives, antibiotics, and antivirals. If we do not know exactly what agents we may be forced to confront, we want mechanisms that can provide broad protection. It would not matter so much. We do not want a bug-specific drug. We want something that can address a wide variety of threats.

This also has direct applicability to another problem. We spent some time talking today about the public health questions which are apart from biodefense. We have a serious problem with microbes becoming resistant to our existing arsenal of antibiotics and antiviral drugs. If we are able to develop broad spectrum therapeutics to anticipate future bioterrorism threats, these are also very important developments we were going to need just to handle conventional health threats.

We have had a report, if I may be so bold as to bring up your counterparts across the water, the British House of Lords, say we may be approaching a pre-antibiotic era. Antibiotic resistance threatens mankind with a prospect of referring to the pre-antibiotic era if these diseases continue to evade the therapeutics we have. We need to do research for that reason alone.

In order to get this broad flexible responsive biodefense capability, we need a lot of research infrastructure. Part of that is the laboratories and the science base that Dr. Fauci described before. A lot of it is tools, methods, assays, reagents, a whole supporting industry of tools and capabilities that are going to make our research in the future better able to be rapidly responsive.

And this is a capability that does not fit directly under Bioshield. We are not going to say we are going to buy one product to provide that capability. That is the kind of capability that is going to come when there is an industry that is developed in response to the demand that we are putting on the mission of getting a more flexible biodefense.

So in terms of the programs we have in place, the NIH programs are very, very important. A basic science base is absolutely important. The Bioshield I investments showing that we need to make connections and provide incentives to industry are also very important. But I think neither of those is sufficient by itself, and we have heard already on this panel some important gaps in that package, one on very important liability concerns: if a firm has a capability but is not willing to bet its future survival on the fact that it may not have been able to anticipate some of the rare sideeffects.

Particularly recognizing that in the case of a therapeutic or vaccine against a bioterror event, we are developing that product for

a situation we really cannot even anticipate today. We do not know what the future bioterrorist event is going to look like so I think liability concerns are even more pressing for biodefense products than we already have in terms of other products.

And we have also had the question of how much incentive is enough for industry, and I guess I would just have to argue, not running a biotech or a pharmaceutical company myself, I am not quite sure what that level is. But I think there is a legitimate concern that the existing incentives may not be sufficient. I am reluctant to raise this story, an anecdote. I am reminded about an argument my parents once had, and I believe they will probably read this in the transcript so I have to watch it. But my mother once said that she really liked Robert Redford in a movie and my dad said no, she did not. It was not that he knew what she liked better than she did, but to his defense, I think he is recalling that she may have said something at the time.

But the point is it does not matter what I think as a sufficient incentive for industry. What matters is what industry thinks is a sufficient incentive, and I think we have also heard about some of the difficulties of having these conversations in a group. I believe there may be some legal mechanisms that under the Defense Production Act or some other means where we can actually hold some. I know the Commerce Department has industry advisory committees where they are able to provide useful collective advice under a Federal Advisory Committee process. So that is an important mechanism I think we should pursue.

Let me just go into some of the overall cautions I want to leave you with before I conclude. One is the other question we have already touched on today, which I think is a very difficult one for a public policy, the degree to which the things we need to develop in the future are restricted to government biodefense missions or the degree to which they may actually benefit a commercial or a private or a public health aspect as well.

In looking for a broad flexible responsive biodefense research base, I think the things we are going to have to build for that are not going to be labeled "government only." They are not going to be labeled "biodefense only." They are going to have to be broad and capable measures, assays, screening tools, licenses that are going to be of benefit to everybody, to the industry as a whole, and I think rather than worry about that and say that is a fault of the provision, I think that is something we need to actually embrace if we want to build a partnership between government and industry and if we want to have an industry that is able to be responsive.

The initial draft of the Bioshield legislation did provide that products with commercial utility were not eligible for Bioshield. That, as I understand, was modified in the last act and the final bill that passed said generic products would be available to Bioshield; however, the commercial utility of the product would be something the Secretary of HHS would have to consider. So we realize there is a tension here. I think that tension is going to get worse because the research supporting capabilities we need are ones that are going to benefit more broadly, and I think we have to encourage that and not be afraid of it.

And, finally, I just do want to leave the last reminder that although we have talked about medical countermeasures today and they are terribly important, that is just one part of our overall defense against the bioterrorist threat, and it is important to address the problem at every stage we can, from dissuading folks who might go down that road to trying to frustrate their ability to collect the materials and technology and expertise. That is a very hard thing to do because the technology is there, but if we can frustrate that, we want to work on it, very important aspect of trying to do what we can to detect these programs wherever they are taking place. And finally increase our ability to respond after the fact.

I would be happy to answer your questions. Thank you.

Senator BURR. Thank you.

[The prepared statement of Mr. Epstein follows:]

PREPARED STATEMENT OF GERALD L. EPSTEIN

Mr. Chairman and members of the subcommittee, I appreciate the opportunity to appear before you today to discuss the capacity to generate medical countermeasures against biological weapons and bioterrorism. I am currently serving as Senior Fellow in Science and Security in the Homeland Security Program at the Center for Strategic and International Studies here in Washington. I also teach a course on science, technology and homeland security in the Security Studies Program at Georgetown University's Edmund A. Walsh School of Foreign Service. I have been working in the area of science, technology, and security policy for more than 20 years and have been studying biological weapons issues and responses for nearly 15 years.

At CSIS, my colleagues and I are launching a major international effort, supported by the Carnegie Corporation of New York and the John D. and Catherine T. MacArthur Foundation, to look broadly at biological weapons threats and to identify opportunities to counter them at all stages, from influencing the intent to produce weapons, to denying access to materials and expertise, to detecting illicit programs, to managing the consequences of an attack. We are also looking at perceptions and threat reduction activities across Nations and across professional communities. The activities to be addressed at today's hearing are an important part of the United States'—and the world's—response to biological weapons threats.

At CSIS I also organized a workshop to examine the global evolution of dual-use biotechnology, looking specifically at the implications of this evolution for the spread of biological weapons and bioterrorism capabilities. The report for this workshop is in press.[1]

I'd like to spend some time this morning discussing aspects of the bioterrorism threat, what they imply for our ability to counter them, and some high priority actions we need to take as a result. Let me set out the following points:

(1) Bioterrorism is a very serious threat, but the details of future biological weapons cannot be known today. Although certain diseases currently pose more serious terrorist threats than others, a wide variety of agents might nevertheless be used, and the exponential growth and dissemination of biotechnology will foster the creation of new ones. Since the time to develop and produce bioweapons agents is, in general, much shorter than the time to develop, license, and produce a response, we cannot rely on hard intelligence alone to direct the development of countermeasures.

(2) Uncertainties about the future threat put a premium on breadth of capability and speed of response. Looking ahead, the most important medical countermeasures are new "broad spectrum" antibiotic and antiviral drugs and other post-exposure therapies. Traditional vaccines have only a limited role in civilian biodefense, because of the time they need to develop protection; we cannot vaccinate our way out of this problem.

(3) Substantially increased NIH biodefense research and the new Bioshield program are necessary components of our national response, but they are insufficient. Further incentives are needed to stimulate production of post-exposure therapeutics and rapid response capabilities, for which we need new research tools and methods.

[1] Gerald L. Epstein, *Global Evolution of Dual-Use Biotechnology: A Report of the Project on Technology Futures and Global Power, Wealth, and Conflict* (Washington, DC: Center for Strategic and International Studies, in press).

We also need to develop animal models for human disease and increased animal production and testing capacity.

(4) Successful incentives that foster biodefense missions could benefit commercial enterprise as well, because many of the necessary supporting capabilities are inherently generic. Policies that attempt to ensure that government incentives or investments apply only to government biodefense missions—as the original version of the first Bioshield legislation attempted to do—are guaranteed to fail at fostering a dynamic, responsive, and flexible biodefense response capability.

(5) Medical countermeasures are very important, but they are only one component of a comprehensive biodefense strategy. Countering bioterrorism also requires efforts to dissuade, frustrate, detect, and counter bioterrorism programs at every possible stage of their planning and execution, not just after an attack has been conducted.

CHARACTERISTICS OF THE BIOTERRORIST THREAT

Importance of Taking the Threat Seriously. As members of this subcommittee no doubt know, history is a poor guide to the bioterrorist threat. There are few areas with so great a gulf between the proven, historical capability to do grievous harm, and the relative paucity of actual attacks. We know for sure that biological weapons, when prepared for effective dissemination in large enough quantities, can kill over large areas. All the necessary capabilities to place many thousands of lives at risk were demonstrated decades ago. We know that the technology, materials, and expertise required to produce biological weapons are available to those terrorists who are sufficiently motivated and skilled to pursue them; essentially all the equipment, materials, and expertise have legitimate application or can be found without great difficulty.

And we know that enemies exist who are eager to kill Americans in vast quantities. What we are not sure of is why we have not yet been attacked in this way. Maybe not enough of today's terrorists took high school biology. Tomorrow's will—and their high school biology classes will be much more potent than today's. We cannot bet our country that whatever restraints have kept terrorists from pursuing this path will persist indefinitely.

Exactly how close terrorist groups are right now to the capability to conduct a major biological attack matters if we want to know how likely it is that such an attack will take place in the near future. However, looking out over the several years that our defensive preparations will take to implement, the details of today's threat are less important than the realization that the rapidly increasing capability, market penetration, and geographic dissemination of relevant biotechnical disciplines will inevitably bring weapons capabilities within the reach of those who may wish to use them for harm (see figure 1).

Difficulty in Predicting or Specifying Future Threats. Given the diversity of potential biological weapon agents and the increasing ability to modify or augment them, either through conventional techniques or genetic engineering, we will never be able to restrict our efforts to a short list of agents considered to be the most serious threats. It is true that certain agents today are considered to pose greater terrorist risks than others because of their combination of health consequences and ease of dissemination. Moreover, a few diseases, such as smallpox and anthrax, pose such dangers that they are worth special attention (smallpox because of its lethality and contagiousness; anthrax because of its lethality and hardiness). However, a wide variety of agents could be used as weapons, and that list will grow over time as science advances, biotechnology spreads, and new capabilities become feasible.

Intelligence collection efforts will not provide a reliable guide for our biodefense activities. First, the "signatures," or observable signs, of a terrorist bioweapons development activity will be very difficult to detect, particularly amidst a large and rapidly growing background of legitimate biotechnical activities. Bioweapons programs do not require large, expensive, or distinct facilities, and we cannot have much confidence that we will spot them.

More serious is the significant mismatch in time scales between attackers and defenders. Unless we radically transform the way we do business—a scientific and technical challenge as much as a management or resource one—our programs to design, develop, approve, and produce medical countermeasures will have lead times that are much longer than those of the terrorist weapons programs they are intended to counter. Today's defensive programs cannot be designed against today's threat but rather must anticipate the threat years in the future—posed by groups and programs that may not even exist today. Moreover, we are unlikely to be able to mount major countermeasures development programs covertly. Attackers will

probably know what countermeasures we are developing and if possible, will work to evade them.

IMPLICATIONS FOR BIODEFENSE

Role of Vaccines. Unavoidable uncertainties in the future biological threat place a premium on broad-spectrum, post-exposure therapeutics and rapid reaction capabilities. Traditional vaccines are less relevant, since they are only effective against specific diseases (and often only against specific strains), and because they generally generate immunity too slowly to be of much value if given after the fact. (Smallpox and anthrax vaccines are exceptions, because they have therapeutic value even if given after exposure). Too many possible other disease threats exist for us to vaccinate our way out of the bioterrorism problem. And we are very unlikely as a society to decide to vaccinate large groups against potential bioterror agents in advance of any attack, since we would not be able to justify imposing the small but nonzero risk of vaccination when we have absolutely no way of knowing what harm—if any—those vaccines will have avoided.

Novel vaccine approaches—such as so-called "DNA vaccines"—are very important because they offer the tantalizing prospect of mounting an immune response fast enough to have therapeutic value post-exposure. However, such vaccines are too speculative to be able to anticipate successful products, or to fit within the 8-year window needed to qualify for Bioshield I funding. Vaccine research might also lead to the development of antibodies to provide quick but temporary protection against a disease during the time needed for a more conventional vaccine to take effect. Even though these techniques would—if successful—provide some "post exposure" response capability, they would still be very specific towards particular diseases.

Need for Additional Antivirals and Antibiotics. Since traditional vaccines are of limited value in responding to an attack, we need antibiotics and antiviral drugs. However, despite their importance for dealing with natural disease outbreaks, let alone bioterror attacks, the development of such anti-infective has been neglected by the pharmaceutical industry in favor of drugs to treat chronic conditions, such as hypertension, cancer, and heart disease. These conditions provide large and continuing markets, whereas most infectious diseases occur only sporadically, particularly in the developed world markets that can readily afford pharmaceutical products. The required course of anti-infective treatment lasts only a week or two, and if successful it clears up the problem—and eliminates the need for further business. Pharmaceutical manufacturers would rather devote their resources to drugs with larger and more lucrative markets—and they would be punished by their investors if they didn't. (As a public policy researcher, I would love to be able to focus my attention on policy problems without considering the financial consequences—but if I am not able to convince a funder to support my expenses and those of my institution, I'm not going to be in a position to work on that topic for long).

A 2004 paper by UCLA researchers finds that, out of 506 new drug candidates that have been disclosed in the development programs of the largest pharmaceutical and biotechnology firms, only 31 represented anti-infectives: 6 antibiotics; 12 antiviral drugs to combat HIV; 5 other antivirals; 5 drugs to combat parasites; 5 to combat fungi; and 1 other.[2]

This dearth of new anti-infectives in the pipeline is especially troubling given the rate at which naturally occurring pathogens are evolving resistance to existing antibiotics and antiviral drugs.

The Infectious Disease Society of America points out that infections that were once easily treatable are becoming "difficult, even impossible, to treat" today. More than 70 percent of the bacteria causing hospital-acquired infections are resistant to at least one of the drugs typically used to combat them. Resistance to multiple drugs is increasing, including resistance to vancomycin, a drug of "last resort." Only two new classes of antibiotic have been developed in the last 30 years, where a class represents those drugs that all utilize the same mechanism to kill bacteria or viruses—and that are all subject to losing their effectiveness as soon as pathogens evolve the ability to evade that mechanism.[3]

---

[2] Brad Spellberg, John H. Powers, Eric P. Brass, Loren G. Miller, and John E. Edwards, Jr., "Trends in Antimicrobial Drug Development: Implications for the Future," *Clinical Infectious Disease 2004:38: 1279–86.*

[3] Quotations and statistics in this paragraph from The Infectious Disease Society of America, *Bad Bugs, No Drugs: As Antibiotic Discovery Stagnates . . . A Public Health Crisis Brews*, July 2004 available online at (http://www.idsociety.org/pa/IDSA Paper4 final web.pdf) accessed February 6, 2005; pp.9,10.

A 1998 United Kingdom House of Lords report concluded that "antibiotic resistance threatens mankind with the prospect of a return to the pre-antibiotic era."[4]

Clearly there is a critical need for new antibiotics and antiviral drugs not only for biodefense, but also to combat naturally occurring infectious disease.

Need for Research Tools, Methods, and Infrastructure. In the long run, we need a vibrant, flexible, and responsive biodefense system that can adapt to threats as they materialize. We cannot mount decade-length; billion-dollar scale vaccine or drug development programs to combat every potential threat agent. Therefore, we must develop research tools that can make a much more responsive system possible. Building such a system will be a tremendous challenge, and there are fundamental scientific questions that will need to be resolved. However, there will certainly be need for tools such as assays for rapidly screening drug candidates; improved methods for determining chemical and biological properties of drug candidates that can accelerate and/or replace certain stages of preclinical testing; bioinformatics approaches to identify promising drug targets; and a wealth of other approaches, including many that are undoubtedly yet to be envisioned.

A major component of this research infrastructure will be improved animal facilities and understanding. Given that many diseases of bioterror concern occur too rarely in humans to permit clinical trials, the Food and Drug Administration has specified that efficacy testing of drugs can be conducted in two different species of animals, rather than humans. However, the "animal models" utilized in these tests must be sufficiently well understood so that the drug's effect on the disease in those animals can be reliably related to how that drug would work against human disease. Development of these animal models; as well as the construction of animal facilities in which these animals can be bred and these tests can be conducted, is a critical biodefense need. Right now, shortages of animals, animal facilities, and animal models threaten to limit and constrain research.

EXISTING GOVERNMENT R&D PROGRAMS AND INCENTIVES FOR INDUSTRY ARE NECESSARY, BUT NOT SUFFICIENT

The Role of the National Institutes of Health. Substantially increased NIH biodefense research funding and the Bioshield program that was enacted last year are necessary components of our national response, but they are not sufficient to generate these post-exposure therapeutics and other essential components of a response to bioterrorism. Important parts of the problem remain unaddressed, such as the research tools and animal model issues described above.

Scientific investments made by NIH have driven the growth of the biotechnology industry over the last few decades, and the very substantial ($1.7 billion) increase in the level of annual NIH funding for biodefense research will improve our basic understanding of disease pathogenesis as well as lay the groundwork for the development of drug and vaccine countermeasures. These investments are also funding substantial increases in "high containment" research facilities that allow scientists to work with dangerous organisms safely. In its traditional role of pursuing the most exciting and productive biomedical science, leaving industry to pick up and run with what it wants, NIH has been tremendously productive. However, this largely "bottom-up" approach is less well suited for a more mission-oriented, product-focused program to filling specific biodefense needs that involve product design and development, clinical trials, FDA approval, scaleup, and manufacturing. Industry's involvement in this process is critical.

NIH research investments will also be essential for bolstering the scientific underpinnings for improved research tools and methods. NIH has developed guidelines that are intended to ensure that research tools, materials, and other resources developed in the course of NIH sponsored research become available to other investigators. However, it is not clear that these guidelines are optimally designed to achieve that end, particularly on the scale that will be needed to support a robust, responsive biodefense capability. The working group that developed those guidelines found that "intellectual property restrictions can stifle the broad dissemination of new discoveries and limit future avenues of research and product development."[5]

Although the group also found that "reasonable restrictions on the dissemination of research tools are sometimes necessary to protect legitimate proprietary interests

[4] United Kindom Parliament, House of Lords, Science and Technology Committee, "Resistance to Antibiotics and Other Antimicrobial Agents," Seventh Report, March 17, 1998, available online at (http://www.parliament.the-stationary-office.co.uk/pa/ld199798/ldselect/ldsctech/081vii/st0703.htm) accessed February 6, 2005; section 1.19.

[5] Federal Register, vol.64, no. 100 (May 25, 1999), p. 28206.

and to preserve incentives for commercial development,"[6] the resulting guidelines do not appear to give sufficient emphasis to the role that commercial firms play in improving, standardizing, distributing, and marketing these tools—and to the corresponding ability that these firm must have to control the distribution of the resulting materials and recoup their investment. I hope that other witnesses at this hearing can provide further information on incentives that NIH and others can offer that will best facilitate the development and dissemination of research tools.

The Role of the Pharmaceutical/Biotech Industry. Pharmaceutical and biotech firms, on the other hand, have not in the past had much incentive to develop products for what are essentially government biodefense markets. Debate leading up to the passage of the original Bioshield legislation last year recognized the importance of engaging these firms, the barriers that had prevented them from participating, and the need to develop new incentives to engage them. Indeed, Congress has appropriated $5.6 billion dollars as of fiscal year 2004 to fund Bioshield purchases, and procurements using these new authorities are now underway. However, it is not clear that these existing incentives will be sufficient, for example, to motivate firms to increase their development of anti-infectives. Given how important it is to augment our existing antibiotic and antiviral arsenal for public health purposes as well as for biodefense, government incentives to stimulate their development—even ones that are not immediately applicable to biodefense—would be appropriate.

The original Bioshield legislation also left gaps, such as the failure to provide liability protection for firms that develop medical countermeasures in good faith the best available scientific and technical understanding notwithstanding, no vendor preparing products to mitigate the consequences of a terrorist attack can ever fully predict the circumstances under which those products would be used, let alone conduct fully realistic tests or evaluations. It will therefore be important to assure firms who are otherwise willing and able to produce medical countermeasures that the threat of product liability lawsuits will not put their survival at risk. An Institute of Medicine Committee that examined DOD's program to develop medical countermeasures against biological warfare agents concluded that "it is important for the government to address industry concerns about product liability risks as part of efforts to accelerate the development of medical biodefense countermeasures."[7]

The SAFETY Act (part of the Homeland Security Act, Public Law 107–296) does provide some liability protection to manufacturers of products to counter terrorist attacks, but it does not apply to products used in anticipation of such an attack, as many medical products might be. Nor does it provide compensation for those who may have been harmed by an antiterrorism product. Therefore, if liability protection is to be provided to shield vendors from unwarranted liability claims, some mechanism going beyond the SAFETY Act—and preferably one that provides compensation for legitimate claims—must be provided.

INADVISABILITY OF DRAWING STRICT BOUNDARIES BETWEEN BIODEFENSE AND COMMERCIAL MISSIONS

At an earlier stage of my career, I directed a study that examined the relationship between military and commercial technologies, looking in particular at the effects and implications of government policies to stimulate one or the other.[8]

It was clear at the time—and it remains true today—that government policies that have the intent—or the effect—of stimulating commercial technology development can be quite controversial. Legitimate objections would be raised to policies that would put government in the position of "Picking Winners and Losers," with the argument being made that the marketplace was much more appropriate than the government in making such a determination. Interestingly, I think that "picking winners" was often a bigger problem than "picking losers." The latter merely wasted money, whereby the former took resources from all of us and had the effect of applying them to the benefit of just a few. Even when such actions were well justified on the basis of their public benefit, the fact that there were private beneficiaries raised issues of equity and fairness.

---

[6] Ibid.

[7] Committee on Accelerating the Research, Development, and Acquisition of Medical Countermeasures Against Biological Warfare Agents, *Giving Full Measure to Countermeasures: Addressing Problems in the DOD Program to Develop Medical Countermeasures Against Biological Warfare Agents*, Lois M. Joellenbeck, Jane S. Durch, Leslie Z. Benet, eds., (Washington, DC: National Academies Press, 2004), p. 80 available online at (http://books.nap.edu/books/0309091535/html/80.html#pagetop) accessed February 6, 2005.

[8] Alic, John A.; Branscomb, Lewis M.; Brooks, Harvey; Carter, Ashton B., and Epstein, Gerald L.; *Beyond Spinoff: Military and Commercial Technologies in a Changing World* (Boston, MA: Harvard Business School Press, 1992).

I revisit this debate because I fear that similar concerns could cripple our efforts to generate a vibrant, responsive, and effective biodefense capability. Some of the most important requirements we face—improved research infrastructure; new tools and methods; new antiviral and antibiotic products; new animal models and facilities—are not specific to biodefense; they apply to biodefense and to commercial missions alike. If we are too concerned about "picking winners"—if we avoid taking actions that might benefit commercial firms, even as they support the biodefense mission—we are guaranteed to fail at developing the capabilities we need. The original Bioshield legislation attempted to do just that, making any product that had a nonbiodefense application ineligible for Bioshield support. Congress wisely eliminated that prohibition before enacting that legislation.

Future actions to support our biodefense capability are similarly bound to raise this same question. Given how generically applicable the necessary capabilities are, we must embrace, rather than avoid, these "dual-use" benefits. Clearly, careful attention will have to be paid to the details in any such incentive scheme to ensure that they are not abused by firms that are not contributing to the biodefense mission, or that are taking advantage of loopholes in the procedures to enrich themselves at the public's expense. But if firms acting in good faith to support the Nation's biodefense mission are unable to benefit in their commercial activities, we are not doing what we need to be doing.

NEED FOR A COMPREHENSIVE APPROACH

Finally, although my comments today have been directed primarily at medical countermeasures to bioterrorist attack, it is important to recognize that we cannot rely solely on after-the-fact responses in dealing with the threat of bioterrorism. As important as they are, medical countermeasures are only one component of a comprehensive biodefense strategy. We must put programs in place to dissuade, frustrate, detect, and counter bioterrorism programs at every possible stage, not just after an attack has already taken place.

One of the chief difficulties in fighting bioterrorism is that none of the measures we can imagine, by itself, can offer high confidence in successfully countering this threat. But by putting a combination of measures in place, or a layered defense—recognizing that each measure or layer has limitations and weaknesses—we can maximize our chances of success.

OTHER USEFUL REFERENCES

Bradley T. Smith, Thomas V. Inglesby, Tara O'Toole, "Biodefense R&D: Anticipating Future Threats, Establishing a Strategic Environment," *Biosecurity and Bioterrorism,* Vol. 1, No. 3: September 2003, pp. 193–202.

Lynne Gilfillan, Bradley T. Smith, Thomas V. Inglesby, Krishna Kodukula, Ari Schuler, Mark Lister, and Tara O'Toole, "Taking the Measure of Countermeasures: Leaders' Views on the Nation's Capacity to Develop Biodefense Countermeasures," *Biosecurity and Bioterrorism,* Vol. 2, No. 4: September 2003, pp. 320–327.

FIGURE 1: Implications of Technology Advance for Bioterrorism

No matter what the actual gap is today between a terrorist group's level of capability in biological weapons and the level needed to do substantial harm, that gap will disappear over time.

ONE-PAGE SUMMARY

(1) Bioterrorism is a very serious threat, but the details of future biological weapons cannot be known today. Although certain diseases currently pose more serious terrorist threats than others, a wide variety of agents might nevertheless be used, and the exponential growth and dissemination of biotechnology will foster the creation of new ones. Since the time to develop and produce bioweapons agents is, in general, much shorter than the time to develop, license, and produce a response, we cannot rely on hard intelligence alone to direct the development of countermeasures.

(2) Uncertainties about the future threat put a premium on breadth of capability and speed of response. Looking ahead, the most important medical countermeasures are new "broad spectrum" antibiotic and antiviral drugs and other post-exposure therapies. Traditional vaccines have only a limited role in civilian biodefense, because of the time they need to develop protection; we cannot vaccinate our way out of this problem with single-disease-specific remedies.

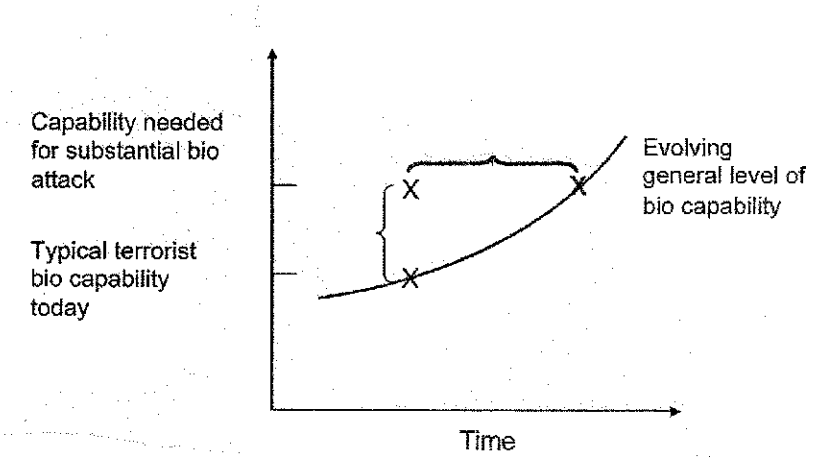
(3) Substantially increased NIH biodefense research and the new Bioshield program are necessary components of our national response, but they are insufficient. Further incentives are needed to stimulate production of post-exposure therapeutics and rapid response capabilities, for which we need new research tools and methods.

We also need to develop animal models for human disease and increased animal production and testing capacity.

(4) Successful incentives that foster biodefense missions could benefit commercial enterprise as well, because many of the necessary supporting capabilities are inherently generic. Policies that attempt to ensure that government incentives or investments apply only to government biodefense missions—as the original version of the first Bioshield legislation attempted to do—are guaranteed to fail at fostering a dynamic, responsive, and flexible biodefense response capability.

(5) Medical countermeasures are very important, but they are only one component of a comprehensive biodefense strategy. Countering bioterrorism also requires efforts to dissuade, frustrate, detect, and counter bioterrorism programs at every possible stage of their planning and execution not just after an attack has been conducted.

FIGURE 1: Implications of Technology Advance for Bioterrorism



No matter what the actual gap is today between a terrorist group's level of capability in biological weapons and the level needed to do substantial harm, that gap will disappear over time.

Senator BURR. The chair will recognize Mr. Cameron.

Mr. CAMERON. Mr. Chairman, members of the Bioterrorism and Public Health Preparedness Subcommittee, I am honored to be testifying before you today on the issue of scientific progress in developing bioterror countermeasures. I am Gordon Cameron, Chief Executive Officer of Acambis. Acambis is a leading developer and producer of vaccines to prevent and treat infectious disease. We employ around 280 people, predominantly in Cambridge and Canton, Massachusetts, although we also have operations in Miami, Florida and Cambridge, UK.

Before I begin, I would like to acknowledge the dedication of the members of this subcommittee to the improvement of current U.S. biodefense preparedness capabilities. In particular, I would like to thank Acambis' constituent senator, the Honorable Edward Kennedy, for his continued support of our smallpox vaccine programs and for his leadership in introducing Project Bioshield together with Senator Gregg. Chairman Burr, we value your leadership on smallpox vaccine compensation so that first responders would be

encouraged to be vaccinated against smallpox. It is with your dedicated leadership, we can ensure the United States and the world can be shielded from the ever-present threat of bioterrorism.

As members of the subcommittee are aware, Acambis' involvement in biodefense has been in the area of smallpox. Under contracts with the Centers for Disease Control, Acambis developed ACAM2000, a new smallpox vaccine with our partner, Baxter Bioscience Vaccines, manufactured over 180 million doses which have been delivered in complete vaccination kits to the Strategic National Stockpile. Extensive clinical trials have been conducted of the vaccine. Acambis has also supplied ACAM2000 to a number of foreign countries also to be used for emergency use stockpiles.

In addition, Acambis and Baxter are developing a weakened smallpox vaccine under contract with the NIH known as MVA. This vaccine is intended for vaccination of the many individuals with skin diseases and compromised immune systems who have contraindications for the use of standard smallpox vaccine.

Acambis is a real-life case study of biodefense policy in action. I thought it would be useful, therefore, to draw upon some lessons learned from Acambis' experience. On the positive side, ACAM2000, that project and that contract have undoubtedly been a major success. Since we were awarded that contract at the end of 2001, we have developed a new vaccine and tested in clinical trials in over 4,000 subjects, both Phase I and Phase II and Phase III clinical trials, and we expect to file a product license application this year.

In addition, we have delivered over 180 million doses to the Strategic National Stockpile. So I think this contract and our performance on it is virtually unprecedented in terms of both scale and in terms of the pace of development and production that took place. As Senator Kennedy pointed out, it was on time and on budget.

So whenever these kind of things happen, we always need to analyze what were the critical success factors in making it happen. I think in the first instance, we had excellent partnership with the U.S. Government and the various agencies. In particular, I would highlight the cooperation we received from the FDA where, unlike a typical periodic review type process of the FDA course of action, we were getting real-time assistance and real-time cooperation, almost daily contact with the FDA, so as issues surfaced, whether they be in the clinical trial design or whether they be in the manufacturing process, we were able to resolve them almost immediately.

Second, in terms of the contractual piece of the contract, we had a very flexible approach to funding in the way the contract was designed. We would get our funded research and development payments on a monthly basis, and that enabled us to in part offset the inherent risk in a development program, but also actually provided some working capital for the large-scale production that was taking place alongside the research and development.

In addition, a technical point of view, the contract permitted fixed price subcontract arrangements with our subcontractors, and through that arrangement, we were able to then draw upon the expertise and capability of our primary subcontractor, Baxter Health

Care Corporation, for whom without a fixed price arrangement would not have participated.

In addition, the way the contract was set up, the government actually procured and paid us for product as we delivered it into the stockpile, irrespective of the fact that it was not actually yet licensed. And that was clearly, you know, advantageous to us, both in terms of cash flow, both in terms of delivering on the final contract.

So I have highlighted some positives and what I would also then do is maybe highlight possible areas for improvement or reflection. We believe, in the first instance, that the final product procurement should be at a level that is consistent with either the original or previously stated goals or policies, and I would cite three examples in this regard: with ACAM2000, there was an intended policy at one point in time to procure 209 million doses of the vaccine, and yet when the final contracts were drawn up, only 182 million doses of the vaccine were ordered. We believe this is in part due to budgetary issues, but the point being that the decision was made relatively late in the day after such time as Acambis had already incurred the cost and the effort to actually work toward the 209 million dose requirement.

Partly related to that is a second issue whereby the first generation vaccine, which many of you are aware was manufactured decades ago on the bellies of calves through a process that would not be acceptable to the FDA today, that vaccine in itself makes up a significant proportion of the smallpox vaccine stockpiled today. And we had previously understood or been led to believe that the old vaccine was being used as a short-term insurance policy until such time as the ACAM2000 product was available.

Over time that policy appears to have changed. ACAM2000 vaccine is now available. However, the first generation vaccine now appears to be a core part of the policy in the stockpile. Granted that it is still effective, but I think in the context of having differentiated products sitting in the stockpile, some unlicensed or unlicensable and some product that is about to be licensed, I think that provides some perception issues for the government.

The third aspect of this we would highlight, on MVA, Project Bioshield and other documentation supporting Project Bioshield has highlighted the need to procure up to 60 million doses of MVA vaccine, but until such time as the RFP comes out for the third contract, we still are not aware of how many doses will actually be procured.

In each of the above three cases, the element of uncertainty has been introduced into the process and actual or potential financial loss has also been introduced. Both of these issues make industry wary and does not help in the government's stringent efforts to try and encourage industry to participate in the biodefense initiative.

The second area of improvement I would highlight would be in terms of the long-term manufacturing arrangements. This is not just about acquiring a stockpile. It is about acquiring a capability over a longer period of time. Very few companies will be interested in putting in all the infrastructure required simply to provide a short-term stockpile and get a short-term return.

All companies are going to be interested over the longer term. So we have discussed over the last several months and years, in fact, with the government the concept of warm-based manufacturing which essentially is ensuring a state of readiness in the production process such that should there be a need to acquire or procure significant additional doses in the event of an outbreak, then there would be a facility ready and available to make large quantities of vaccine.

This concept is consistent with what the World Health Organization outlined recently in its smallpox vaccine initiative where it declared that it wanted to have at least two sites around the world capable and ready to produce smallpox vaccine at short notice. We are clearly one of those suppliers.

But I think we need to learn from the lessons from the past here where in the case of smallpox vaccine, production ceased in the early 1980s because there was no defined market. So creating the market through a warm-based manufacturing approach which would essentially involve annual production runs and the government procuring vaccine on an annualized basis would serve both parties well. The government would have a state-of-readiness facility available to it for the company to produce vaccine. The company would have a longer term revenue arrangement which in itself would be attractive.

In our case, we are still awaiting confirmation. We have submitted a proposal to the government for a warm-based manufacturing proposal over the longer term and we still await both confirmation and budgetary approval for that particular process. Each of that adds to this issue of uncertainty for the contractors that are highlighted above.

Finally, I will just refer to the issue of manufacturing generally. The topic of this hearing is scientific progress. On that subject, it is all too easy to focus on the research and development aspects. Much has already been done to support innovative research in the area of biodefense. This is only part of a much larger and much more complex picture if scientific developments are to bring real benefits. In particular, I refer to manufacturing.

There is little point in developing a countermeasure if it cannot be made at the required scale. Incentives should be applied as much to production as to research and development of countermeasures. Acambis has been a proud and willing participant in the biodefense arena to date. However, Acambis' and other companies' willingness to participate or continued participation is dependent upon a stable commercial arrangement for manufacturing and upon government commitment to stockpiling contracts and production readiness or warm-based programs.

Without these, the scarce and highly valuable resources and capabilities of companies such as Acambis will be deployed in other areas that are more commercially attractive, leaving the government less able to fulfil its stated policy commitments. Mr. Chairman, members of the subcommittee, I thank you once again for inviting me to speak today and I am happy to answer any questions you may have.

Senator BURR. Thank you so much and thank all four of you for your testimony.

[The prepared statement of Mr. Cameron follows:]

PREPARED STATEMENT OF GORDON CAMERON

TESTIMONY SUMMARY

Acambis is a leading developer of vaccines to prevent and treat infectious diseases, employing around 280 people in Cambridge and Canton, Massachusetts, Miami, Florida and Cambridge U.K.

Under contracts with the Centers for Disease Control, Acambis developed ACAM2000, a new smallpox vaccine and, with our partner, Baxter Bioscience Vaccines, manufactured over 180 million doses, which have been delivered in complete vaccination kits to the Strategic National Stockpile. In addition, Acambis and Baxter are developing a weakened smallpox vaccine under contract to the NIH. Designated as MVA, this vaccine is intended for vaccination of individuals with skin diseases and compromised immune systems, who have contraindications for use of standard smallpox vaccine.

The incredibly rapid pace of the vaccine development program for ACAM2000, which will break all existing records for time to receive FDA licensure and for the scale of vaccine supply, was in part due to our unique partnership with the Federal Government. The Federal Government worked closely with Acambis to minimize risk and drive development from the laboratory through large-scale manufacturing and clinical trials.

At the same time, our private-public partnership taught Acambis that government support at the development stage of production, while contributing to the rapid deployment of ACAM2000 to the Strategic National Stockpile, was an insufficient precondition for Acambis to realize the full benefits of our mutual investment with the Federal Government. What was needed was a stable and commercially viable funding arrangement for sustainable manufacturing, not just for the "now" but to secure supplies for the future. Consequently, our willingness to develop new countermeasures relies on the availability of this arrangement.

Lessons learned include: (1) The final dose order should be consistent with original plans negotiated between the manufacturer and Federal Government; and (2) The government should provide for a production readiness arrangement, otherwise referred to as "warm-based manufacturing." This policy involves continued funding to support a minimum level of annual production, to strengthen domestic preparedness for a smallpox emergency, while providing an incentive to build and maintain a specialized facility for biodefense vaccine production.

It is necessary that manufacturers of biodefense countermeasures have stable and commercially viable funding arrangements for manufacturing to ensure continued scientific progress because: (1) Vaccine manufacturing is associated with tremendous risk and cost. **Without the appropriate incentives for manufacturing, our facilities and technological know-how will be used for purposes other than biodefense;** and (2) there is an enormous need for scientific progress with other bioterrorism agents. Because of the benefits of advanced science, the U.S. Government must encourage innovation of new production methods such as cell-culture to improve domestic preparedness for biodefense **and** infectious disease.

Mr. Chairman, members of the Bioterrorism and Public Health Preparedness Subcommittee, I am honored to be testifying before you today on the issue of scientific progress in developing bioterror countermeasures. I am Gordon Cameron, CEO of Acambis. Acambis is a leading developer of vaccines to prevent and treat infectious diseases, employing around 280 people in Cambridge and Canton, Massachusetts, Miami, Florida and Cambridge U.K.

Before I begin, I would like to acknowledge the dedication of the members of this subcommittee to the improvement of current U.S. biodefense preparedness capabilities. In particular, I would like to thank Acambis's constituent Senator, the Honorable Edward Kennedy, for his continued support of our smallpox vaccine programs, and for his leadership in introducing Project Bioshield together with Senator Gregg. Chairman Burr, we value your leadership on smallpox vaccine compensation, so that first-responders would be encouraged to be vaccinated for smallpox. Senator Gregg, I would also like to applaud your introduction of S. 3 along with your colleagues, Senate Majority Leader Frist and Senators Sessions, DeWine, Santorum, McConnell, DeMint and Allen. It is with your dedicated leadership that we can ensure the United States—and the world—can be shielded from the ever-present threat of bioterrorism.

Mr. Chairman, members of the subcommittee, among all of the diseases that could be used for bioterrorism, smallpox is widely acknowledged to be by far the greatest threat. Not only is it a fearsome disease, killing over one-third of those afflicted, but it is contagious and if introduced, could spread rapidly across the Nation and the world. Nearly half the world population has no immunity to smallpox, since routine vaccination ceased 30 years ago. Two dramatic table-top exercises, "Dark Winter" conducted in June 2000 and the recently completed "Atlantic Storm," have demonstrated the global impact of a bioterrorist incident, highlighting the widespread economic and societal devastation it would provoke around the world. The eradication of smallpox remains one of the world's greatest medical achievements, but knowing that the former Soviet Union developed smallpox as a strategic biological weapon, and fearing that stocks of the virus could have spread to other former Soviet States or even to terrorist groups, it is essential that the world prepare against the possibility of its return.

Currently, vaccines offer the only realistic countermeasure to smallpox. Under contracts with the Centers for Disease Control, Acambis developed ACAM2000, a new smallpox vaccine and, with our partner, Baxter Bioscience Vaccines, manufactured over 180 million doses, which have been delivered in complete vaccination kits to the Strategic National Stockpile. Extensive clinical trials have been conducted of the vaccine. Acambis has also supplied ACAM2000 to a number of foreign countries for emergency-use stockpiles.

In addition, Acambis and Baxter are developing a weakened smallpox vaccine under contract to the NIH. Designated as MVA, this vaccine is intended for vaccination of the many individuals with skin diseases and compromised immune systems, who have contraindications for use of standard smallpox vaccine.

Scientific Progress: Cell-Cultured Smallpox Vaccine

Even before the terrorist attacks on September 11, 2001, the CDC recognized that the U.S. stockpile of smallpox vaccines had to be augmented and updated. In September 2000, it awarded Acambis a contract to develop a new smallpox vaccine, and to manufacture and maintain a stockpile of 40 million doses.

The objective of this contract was to develop a modern equivalent to the old smallpox vaccines that were used so effectively in the worldwide eradication program while taking advantage of state-of-the-art cell-culture manufacturing technology, equipment and processes. Vaccine manufacture has come a long way since the old vaccines were produced from the skin of cows. Cell-culture manufacture allows for production of a 21st century product, consistent with Good Manufacturing Practices, free from concerns about potential animal-related contaminants, and capable of being produced more rapidly and in larger quantities.

The U.S. Government has a clear policy to maintain a stockpile of smallpox vaccine sufficient to vaccinate every man, woman and child in case of a smallpox outbreak. The 182.5 million doses of ACAM2000 we successfully delivered to the Strategic National Stockpile represent only part of the U.S. stockpile. The balance is comprised of two brands of animal-derived smallpox vaccines, and we understand that the government has reserved 20 million doses of these vaccines for use by World Health Organization in case of an outbreak in a foreign country.

Mr. Chairman, Acambis believes that all citizens should have access to the most technologically advanced smallpox vaccine available, which is ACAM2000. Following extensive clinical testing, ACAM2000 will shortly be reviewed for licensure by the FDA, which has identified it as a product for fast-track regulatory review. Moreover, we support a policy that would make this modern cell culture-derived product, particularly if it is licensed by FDA, available to our friends and allies through the auspices of WHO, rather than the antiquated cow skin-derived vaccine.

As members of the subcommittee are well aware, concerns about the lack of countermeasures extend far beyond known bioterrorism agents and covers a long list of infectious diseases. Nature has been the most efficient purveyor of new biological threats, such as pandemic influenza, SARS and West Nile. I would submit that because of the benefits of advanced science, the U.S. Government must encourage innovation of new production methods such as cell-culture to improve domestic preparedness for biodefense **and** infectious disease.

Ensuring Continued Scientific Progress of Biodefense Countermeasures

Mr. Chairman, I would like to highlight the incredibly rapid pace of this vaccine development program, which will break all existing records for time to receive FDA licensure and for the scale of vaccine supply. A key element of technical progress was our unique partnership with the Federal Government. From the beginning, the Department of Health & Human Services, the CDC, and in particular the FDA's Center for Biologics Evaluation and Research worked closely with us, thereby mini-

mizing risk and driving development from the laboratory through large-scale manufacturing and clinical trials.

Three specific government actions were instrumental in moving our vaccine development program forward. The first involved a flexible approach to funding, particularly the form of monthly installments for research and development funding, which helped to maximize flexibility and alleviate the myriad of risks associated with accelerated product development. The second relates to the FDA's willingness to monitor all aspects of the manufacturing, control, and clinical development on an ongoing basis instead of upon completion of all studies. With FDA's real-time assistance and cooperation, Acambis was able to successfully develop manufacturing plans for ACAM2000. Finally, the willingness of HHS to view subcontractor relationships as commercial fixed price efforts allowed Acambis to utilize large healthcare companies—with proven infrastructure and supply chain capabilities—to perform important facets of the program.

I can say with all certainty that we would not have a partial U.S. stockpile of cell-cultured smallpox vaccines without the hard-work and dedication of our government and partners, particularly during the critical years following September 11.

At the same time, our private-public partnership taught us that government support at the development stage of production, while contributing to the rapid deployment of ACAM2000 to the Strategic National Stockpile, was an insufficient precondition for Acambis to realize the full benefits of our mutual investment with the Federal Government. What was needed was a stable and commercially viable funding arrangement for sustainable manufacturing, not just for the "now" but to secure supplies for the future. Consequently, our willingness to develop new countermeasures relies on the availability of this arrangement.

Allow me to provide you with two examples from Acambis' experience to highlight instances where the funding arrangement for manufacturing could have been made more stable and commercially viable to encourage continued scientific progress in biodefense.

First, it is important that the final dose order be consistent with original plans negotiated between the manufacturer and Federal Government. In the case of ACAM2000, in initial discussions, the government had expressed an intention to order 209 million doses for the U.S. Strategic National Stockpile. In the end, the government ordered 182.5 million doses, in part, we believe, due to budgetary constraints. Acambis, as the contractor, had been working towards the 209 million dose goal, so was both surprised and disappointed by the government's decision. Acambis also suffered financially, as the investment made, largely in good faith, did not yield the expected return. This type of a scenario is exactly what dissuades many industry players from participating in the biodefense business. It is also unfortunate that it comes at a critical time when government is making extensive efforts to attract industry to participate in supporting its Biodefense initiatives.

Second, the government should automatically provide for a production readiness arrangement, otherwise referred to as "warm-base manufacturing." This involves continued funding to support a minimum level of annual production, once the initial stockpile requirements have been sent to the Strategic National Stockpile. The ACAM2000 contract did not establish funding for a specific program.

From a biodefense standpoint, warm-base aims to strengthen domestic preparedness for a smallpox emergency. The lead time associated with reinstating manufacturing for the smallpox vaccine is anywhere between 6 and 8 months, and could be several years if the trained personnel, validated equipment, and entire production train were allowed to fall into disuse. The warm-base program enables the manufacturer to provide a "turn-key" operation, should an outbreak occur or demands for production increase.

From the manufacturer's point of view, warm-base manufacturing provides an incentive for the tremendous investment and compliance costs associated with building and maintaining a specialized facility for vaccine production. For example, in preparing to manufacture ACAM2000, we modified facilities with specific capabilities for handling the live smallpox virus, which took nearly 4 years to complete.

At the end of the warm-base program, the government would have an adequate stockpile to ensure domestic preparedness, and the manufacturer would have been able to justify its investment. The Executive Board of the World Health Organization recently highlighted the importance of a warm-base manufacturing arrangement in a report on the Global Vaccine Stockpile Reserve (dated December 23, 2004), citing the need for not one but two active manufacturing locations in the world.

Since it is Acambis' intention to file a Biologics License Application for ACAM2000 in 2005 for FDA licensure, a warm-base program would allow for steady replacement of the older vaccines with ACAM2000. Once the smallpox vaccine stock-

pile is fully FDA licensed, the government would no longer need to be concerned with informed consent or issuing orders under Bioshield, which would ultimately speed up the process of vaccination in the event of an attack.

Acambis presented a recommendation for warm-based manufacturing to the CDC in December 2004, and is currently awaiting a decision on whether the distribution of fiscal year 2005 funds will permit the CDC to finance this request. However, a contract that only spans 1 year is insufficient to warrant the investments we must make in warm-base manufacturing. To be certain that our government is ensuring adequate biodefense preparedness and an incentive for continual investments into our smallpox vaccine facility, a more long-term arrangement is necessary. Acambis has requested an extension of this program to the CDC with funds to be appropriated in the fiscal year 2006 cycle.

The Need For Stable and Commercially Viable Funding Arrangements

Why is it necessary that manufacturers of biodefense countermeasures have stable and commercially viable funding arrangements for manufacturing to ensure continued scientific progress? Allow me to expand on these issues and provide the subcommittee with a sense of lessons learned from our public-private partnership.

First, as I suggested earlier, vaccine manufacturing is associated with tremendous risk and cost. There are many companies ready and willing to engage in early stage research for biodefense countermeasures, but very few have the expertise, experience, and facilities necessary to manufacture and deliver the vaccine. Acambis and our partner, Baxter Vaccines, wish to be part of this manufacturing base, **but without the appropriate incentives for manufacturing, our facilities and technological know-how will be used for purposes other than biodefense.**

At this point in time I would like to emphasize to members of the subcommittee that, for biodefense countermeasures such as our ACAM2000 and MVA smallpox vaccines, our sole customer is the government. As such, we rely on a private-public partnership that acknowledges the unique concerns of our industry and encourages progress—not only from research and product development to manufacturing, but also from manufacturing to the final sale, in this case the Strategic National Stockpile. Thus, continued scientific progress for biodefense can be achieved if the manufacturer is presented with options that intend to make the investment in production stable and worthwhile through support for product industrialization or commercialization.

Secondly, Mr. Chairman, there is an enormous need for scientific progress with other biodefense countermeasures. For example, as much as 20 percent of the U.S. population—60 million people—could suffer from serious or potentially fatal adverse reactions if vaccinated with the current smallpox vaccines in the case of an actual or threatened smallpox outbreak. As part of Project Bioshield, the government has recognized the need to protect this vulnerable population, which includes individuals with compromised immune systems, HIV and skin diseases, particularly eczema. Through contracts with the National Institutes of Health, Acambis is now developing an attenuated smallpox vaccine, known as MVA, intended for use by this subpopulation.

A final solicitation to acquire this vaccine for the Strategic National Stockpile is expected in 2005 under Project Bioshield. If the value or size of this solicitation were to be below the 50 to 60 million doses originally projected by the NIH and the Congressional Budget Office, it may be difficult to dedicate staff and facilities to the project at the cost of pursuing other commercial opportunities, **and it would certainly make other manufacturers wary of committing to develop countermeasures to other bioterrorism agents.** Most importantly, such a decision would leave a huge segment of the population without access to the vaccine they need.

Acambis recognizes that the government must strike a balance between prudent government purchasing and the multi-year cost to build a domestic industrial base for biodefense products. Mr. Chairman and members of the subcommittee, you are undoubtedly aware of the difficult position America faced last year because it was dependent on a foreign manufacturer of influenza vaccine. Strategically important vaccines against epidemic diseases, such as smallpox, should be made in the United States and not be subject to foreign control or dependent on regulatory oversight of other countries. To achieve a viable domestic capacity, however, the government must provide adequate incentives for manufacturing. Acambis, as one of the few companies with the capability to perform this activity, is willing to work with the government to devise a solution that manages government costs while sustaining a domestic biodefense readiness capability.

Concluding Remarks

Having stood at the frontline of biodefense work in the United States to date and, in many areas, blazed a trail for other companies, Acambis has developed a unique insight into this vital area. My testimony today has focused on just one aspect of countermeasure production where improvements are needed to ensure continued scientific progress and the growth of a viable domestic industry. Other aspects include a review of liability and regulatory provisions, particularly concerning the animal model for testing and possibly tax credits.

Much is already being done to support innovative research in the area of biodefense, but this is only part of a much larger and more complex picture if scientific developments are to bring real benefits. Incentives should apply as much to production as to development of countermeasures. Acambis has been a proud and willing participant in the biodefense arena to date. However, Acambis' and other companies' continued participation is dependent upon a stable, commercial arrangement for manufacturing, and upon government commitment to stockpiling contracts, and production readiness or "warm-base" programs. Without these, the scarce and highly valuable resources and capabilities of companies such as Acambis will be deployed in other areas that are more commercially attractive, leaving the government less able to fulfill its stated policy commitments.

Mr. Chairman, members of the subcommittee, I thank you once again for inviting me to speak to you today and would be happy to answer any questions you may have.

Senator BURR. At this time, I would recognize the chairman of the full committee, Senator Enzi.

The CHAIRMAN. Thank you, Mr. Chairman. Dr. Painter, you run a small company based in North Carolina and I think to have a strong biodefense policy for the United States, we are going to have to involve a lot of small companies. I am from Wyoming where we do not have a single big business headquartered, and I run a small business. I know that the Federal Government sometimes needs to be reminded that small companies do not have all the specialists that big ones do and it can be a little bit more difficult for them to make it through the maze.

From your perspective, what does HHS need to do to ensure that small companies like yours understand how to work with the government or can you suggest some ways to make it easier to work with the government?

Mr. PAINTER. Yes, Senator, that is a good question. From our perspective, some clarity with regard to the nature of the market. We recently went out and borrowed a significant amount of venture money, and with that venture money, we can contract expertise. So we can leverage our capacity to do development, but the problem is we cannot tell the people we are borrowing from how much smallpox drug the government might want to procure because we do not understand how it would be applied nor is there an overall process visible to us or a strategy for using the drug in the event of attack.

So we do not know the market size. Furthermore, because of the problems associated with the animal model, we cannot tell investors the time to approval to sale. So without clarity, we cannot answer the two critical questions that drive risk determination in venture investment. So any clarity that can be offered there will be of profound importance to our being able to stay viable and get the countermeasure made.

The CHAIRMAN. Thank you. As you think of more of them, convey those to us, too, because we want to be sure that small business has a part in this. There is usually a lot more flexibility and quick-

ness to adapt to the market from small businesses than there are from big ones, so we want to encourage that.

Dr. Abramson, you called for no fault liability protection systems for bioterrorism related to the vaccines that cover the manufacturers and health care workers. You suggested the compensation system that would cover medical expenses and lost wages but not punitive damages. Do you believe this type of protection is also important for the therapeutics that treat these infections caused by these same agents?

Dr. ABRAMSON. I think many of the issues are the same, Senator, and a lot of times I would foresee us using drugs that are nonFDA approved at all, forgetting age and indication, but then we would be using them on a mass scale, and every drug, every therapeutic we have has side effects, and somebody, not one person but multiple people are going to be adversely affected.

In a lot of ways, they're willing to take the vaccine, to take the medicine helps protect the next person in society, and so the people who do not do it we call sort of freeriders, and you cannot have that in a mass emergency outbreak whether it is a bioterrorist attack or not. So I see a lot of the same issues. And I would call for the same measures.

The CHAIRMAN. OK. Thank you. Dr. Epstein, what would you say to those who believe that additional incentives to produce bioterror agents would just be a windfall to the biomedical research community or the pharmaceutical industry?

Mr. EPSTEIN. I think across the board incentives for anything are something one has to look closely at, and I do worry that if there is an incentive program and someone says, you know, if we hang another molecular group on the end of this drug, we can call it a new product and get another incentive. So the details will matter. The incentives have to be ones that actually get the benefits we want.

I personally, think that new, particularly a new broad spectrum, a new class of antibiotic would be something I think is very valuable, and by class of antibiotics, we have, each antibiotic works by interfering with some mechanism in a pathogen. It shuts off this particular molecule. You can have a lot of variations of drugs that basically work on the same principle but have different properties in the body, so a whole family of drugs take effect at different speeds or they have different dosages, but they all work on one basic mechanism. Once the bugs figure out how to block that drug, all the drugs in that class are gone, and we do not have very many classes of antibiotics. If we had a new class, that means all the drugs that are already out there working against microbes that have found resistance to them, a new category of drug is one that those bugs would not be resistant to.

So something that would provide a new class of drugs or a major increase in our therapeutic ability is something I think we need. So I do not consider that a windfall. One does have to worry how the incentive is actually worded in detail, and by the time the lawyers get done with it, I do not want someone figuring out how to make a huge amount of money without really making a contribution. So that means the details are going to matter.

The CHAIRMAN. Thank you. Could I ask a couple more questions?

Senator BURR. Absolutely.

The CHAIRMAN. Or would you prefer I did it in the second round?

Senator BURR. Go ahead.

The CHAIRMAN. Thank you. Dr. Epstein, you mentioned that of the 506 therapeutic candidates that there are really only 60 that are being worked on now. Would you consider with the bioterrorism threat that is facing this country what number of anti-infectives would you like to see in the pipeline to indicate that we have a strong biodefense?

Mr. EPSTEIN. Senator, I think the number was six. Of the 500 and something new candidate molecules or drugs, six antibiotics and a smaller number of antivirals are in the pipeline. I do not know what the right number is, but I do know that the incentives facing the industry do not lead them in this direction because when you have an infection and you take an antibiotic for it, in 2 weeks, if you are lucky, it is cleared up, and you are no longer a customer. So what makes much money for the drug companies is a chronic condition where you will be taking medication for the rest of your life, and I cannot fault the companies for saying that is a better return on their investment, and if they decided to do differently, the stock markets would probably punish them for it.

So I do not know what the right number of anti-infectives and antibiotics is, but I do think that we are not going to get enough if it is just left to the market. I think we do have to provide an explicit attention to increasing the number of new drugs and therapeutics.

The CHAIRMAN. Thank you. One quick question for Dr. Cameron. I could not help but notice that all of you in your statement had something dealing with liability protection. Could you expand a little bit more on what you are talking about with the liability protection particularly?

Mr. CAMERON. Well, in the context of ACAM2000, our contract, we were able to secure liability protection through a number of different efforts, the original contract and then subsequently through legislation. So from our perspective, that box was ticked, and it had to be ticked. It was a precondition effectively toward taking on the contract. So all I would say in that regard is we were okay in ACAM2000. I would just encourage to make sure that all the other countermeasures thereafter follow a similar pattern.

The CHAIRMAN. Thank you. Thank you, Mr. Chairman.

Senator BURR. Thank you, Mr. Chairman. Let me follow up on that, Mr. Cameron, if I could. Without that box being checked, without the total liability, could you have moved forward as a company?

Mr. CAMERON. We would not have.

Senator BURR. Would not have?

Mr. CAMERON. No. Quite simply, we are a public company with stockholders. They would not have accepted that potential risk nor would we as a board of directors and as a company.

Senator BURR. So any company in a similar situation is going to weigh risk in relation to the guaranteed sale. In this particular case you might have ended up short of what you thought, but there was a revenue projection that you were able to match with that.

Mr. CAMERON. Yes, I think all companies will assess risk in whatever investment proposal they are looking at and trying to define the risk associated with potential use of unlicensed smallpox vaccine.

Senator BURR. Is there anybody within the world of manufacture out there that is going to look at it any differently?

Mr. CAMERON. I can only speak for us. But if I was a responsible leader of my company, I think I would look pretty carefully. I think you need to obviously look at the profile of the product and the likelihood of it actually being utilized. I think clearly the smallpox vaccine, it had a history of adverse events, so in that context then we needed to be extra, extra vigilant. But it may well be with some other countermeasures or other products where the risk is deemed to be lower.

Senator BURR. Does Acambis have any restrictions placed on them for the sale of this product outside of our government's contract?

Mr. CAMERON. We are allowed to sell, as I highlighted actually in my testimony, we have been and are allowed to sell our product around the world and have sold to around 13 countries outside of the U.S. We are not allowed to sell to the private market in the U.S. unless it has an ACIP recommendation, but that is the only restriction per se, although the control and the distribution and the sale of the product outside of the U.S. is actually under the guise or control of the FDA. So they are fully informed and fully involved in that process.

Senator BURR. You talked about the wonderful job that FDA did in this fast track approval process or fast track process. Did FDA have individual FDA employees on site in your facility?

Mr. CAMERON. There is a time they did. Yes, the interaction was a mixture of people on site or regular telephone conferences or whatever. I think the point is it was real-time interaction so any issues that surfaced, and they did—issues do surface as you go along—were able to be resolved in a very timely manner rather than the typical process where they would come in once every 12 months and visit a plant or visit a facility or have a telephone conference.

Senator BURR. Is it safe to assume that a majority of their concerns dealt with the manufacturing process?

Mr. CAMERON. It is twofold. The issues were related to manufacturing and the whole design of the clinical trials and the protocols associated with them. There was a lot of interaction with them, and then from a safety perspective as much as anything else.

Senator BURR. Dr. Painter, some have referred to the changes in this FDA fast track as we did it in the legislation, that they look at that with great fear, that a small change might become a large change, might become disastrous to the rest of what FDA does. You mentioned the need for improved animal models and offered a two-part solution. Can you give us any more details about the solution, both the working groups and the incentives for companies to participate in the development?

Mr. PAINTER. Yes, sir, that is a difficult question. In the case of utilizing animal models to try to develop a therapeutic, it is unprecedented. I have worked many years on Hepatitis B and C, HIV.

We always had animal models, but those models were to give an indication of activity in a living organism, not to provide data for registration.

So as this idea of the animal efficacy rule gets reduced to practice, the majority of questions that have come back to us from FDA are relating to, is how do you know the model is relevant? So there is going to have to be a lot of time and effort put into that, and I think that private companies should be incentivized to take on the challenge, and somehow there would be a mechanism where they can gain revenue by improving the model.

Working groups—the NIH has some of them. It is interesting that a lot of the questions that are really relevant to proving that a drug works, only evolve out of the interaction between an FDA regulatory panel and the sponsor of the drug. So as the vanguard goes through and the key questions get asked, they need to be taken back to really real-front line working groups to try to take the issues and reduce them to practice so that we can move the indication forward.

That may not be a very satisfactory answer. I cannot be very crisp. We are doing this in real time. And it has really only been in the past 3 or 4 months that we have begun to understand the questions from the FDA. How do we provide guidance to a physician from efficacy in drug distribution data in a mouse? And it may not be the right virus. We do not know what viruses were weaponized. At what rate does that virus replicate in the blood. We have to get some answers.

Senator BURR. Without that flexibility of changes, could you even move forward?

Mr. PAINTER. No, we need flexibility and I must say that I am encouraged by the degree of flexibility and the dedication and the interactions we have had with the people at the NIAID, the people in academia, and we have had the same experience. The CDER regulatory people at FDA have responded to us in real time which is unprecedented.

Senator BURR. I would mention to all of you the further we get away from September 11, 2001, the greater concern I have with our ability to have a long-term program that addresses us in the same fashion as we are learning today as we try to go out and get these enacted. It is safe to say that if today you were at a point with your antiviral and we had a smallpox attack, if the Federal Government said for the sake of mortality, we want to go ahead and give this to people, you are protected from liability when they make that decision based upon some acts we have already done.

If you were not doing what you are, if there was no company out there, sort of in the antiviral world for smallpox, what would happen?

Mr. PAINTER. I think we would lose a lot of our citizens. There would not be a capacity to respond.

Senator BURR. Does this debate, this decision that we have got in Congress, does it come down to that that is black and white?

Mr. PAINTER. The question that we are constantly asked, particularly by investors, is they want to discount our value based on attack probability. Is there going to be an attack? There seems to be a wide range of opinions. If the attack is using smallpox, if there

is a high probability, and that is known, then I think we should move heaven and earth to do anything that is possible to get every countermeasure on line so that we have antivirals to augment vaccines.

Senator BURR. Let me ask any of you about what I would call and some of you have dual use products, those that might be applicable to a particular area of concern that we have from a bioterrorist standpoint, that either up front we know or later on we learn, that they have a commercial marketplace for them.

And rather than ask you specifics or to be general on how we deal with them, let me ask a specific if I could. Is it conceivable that were we to come up with a set of incentives for those products to enter our system, could we have a separate regimen for those same products introduced into the commercial stream? In other words, were we to extend patents on this side, could we, in fact, mirror existing patents on the commercial side were we to choose to do that?

Mr. PAINTER. I would like to jump to the mike on that one. We have the possibility of dual use in the smallpox drug. And I would like to add that to Dr. Epstein's challenge to have broad spectrum antiviral agents, if one can indeed find such an agent, and they are very rare, there is only one that I know of right now, then in all probability its applicability will extend beyond the weaponized to more common needs for antivirals.

So in order to have success, as he asked for, then we will indeed have this issue. Certainly, anything that will incentivize and provide additional opportunity for companies, particularly now, for dual use, where there are at least perceived to be quite large uncertainties on the commercial side by investors, would incentivize not only people to stay, but give them a way to live through some of the uncertainties and ups and downs as we try to answer the questions like the animal model that we have to get past.

If on a parallel path, we can keep a commercial product going, then the company can remain viable, and I might add that any experience you get either on the biodefense side or on developing a drug for a commercial use, you can leverage that to expedite development on either side.

So these two uses are intertwined and when you confine them, I think they need to be encouraged, not discouraged or looked upon as a liability.

Mr. EPSTEIN. Mr. Chairman, let me add to that. I think clearly today we can say there is a difference between commercial products and biodefense products. Commercial products are the ones that have been on the market and the biodefense products have not, and we have had a short list of bio-threat agents we have been working on because there are a couple that are so much worse than others—we say smallpox and anthrax, and let us start there. And then you get a very long list. We have a Category A, but nature does not draw sharp lines, and I think as we go into the future, it is going to be harder and harder to say what is biodefense and what is public health.

If we have SARS and it gets distributed as a weapon. Even the term "weaponized" really dates back to military conflict where you have to make a bug that can be spread over a battlefield and stay

alive when it goes 20 kilometers downwind. If you are in a shopping mall with a perfume sprayer, is that weaponization? I think the era we are getting to gets back to what I was saying, the inability of firm intelligence to really guide us with specifics and a corollary to that is the inability to draw some of these sharp distinctions, and I think it does pose a real problem if public policy tries to treat biodefense differently than public health or than commercial products.

It is going to, again, now we can do it. The first Bioshield results did that. But it is going to be harder and harder to keep those straight as we go on, and I think it will probably mislead us and maybe get us to the wrong answer.

Senator BURR. I said at the beginning I thought one of the obligations we had was to be ahead of the curve so even though there may be some people behind me that are cringing as I ask that question, why are you going there, why would you get into this now, I think it is real important that we talk about it. And it means something different potentially to somebody in academia than it might mean to a CEO of a company that is very reliant on the capital markets to finance tomorrow and next year and the year after, and for somebody like Mr. Cameron who may already be out there, might already have this experience of some type of dual markets, there is some light that can be very important to us as we head down this road.

Dr. Abramson.

Dr. ABRAMSON. I think influenza is the prime example of the blurring of this issue. So H5N1 is sitting over in Asia and is one, probably one, genetic mutation away, whether it is weaponized by somebody or just occurs in nature from being able to be transmitted person to person. So you have an extremely virulent organism that when it does get into a person kills them at a very high rate, somewhere in the range of about 50 to 70 percent, and it is one small mutation away from being able to be a true mass pandemic. And I see a lot of trouble in trying to split hairs here in differentiating something like that.

Senator BURR. Well, you spoke specifically to the liability issue, and let me ask you to elaborate a little bit more. There are some that believe that current law provides a sufficient protection or assurance for a robust interest of companies to become involved. Dr. Fauci and I focused on the word "robust," and I am not sure that we know, in fact, in this spirit what the definition of it is yet. I think you explained very well that Bioshield ultimately cannot be successful——

Dr. ABRAMSON. That is right.

Senator BURR [CONTINUING]. Unless we address liability. Specifically why?

Dr. ABRAMSON. Well, again, I will use the H5N1 as an example. I do not see a company willing to be able to produce that product or drugs that are needed against that product, because some of the antivirals that we have against influenza do not work against that particular bug, without knowing that—if it is going to be used for millions and millions, and I mean literally that many people, there will be side effects that are true, and there will be side effects that are associated, and there is going to be an extremely high risk from

a legal standpoint that the company is going to have to assume—and I do not see companies willing to do that. I have had lots of discussions in trying to think about pandemic flu about this, and I get no sense that they really want to step up to the plate and take on this risk without that kind of protection.

Senator BURR. Let me once again thank our witnesses and let me say to Dr. Painter the question you have raised as it relates to Soviet scientists, the collaboration, if we are not aware of the answer to the question you raised, I can assure you that it is something that we will pursue and hopefully Senator Roberts as well will pursue that from an avenue of other committees, specifically Intelligence that he has the chairmanship of.

As I said at the beginning, I see this as the first of several hearings that enable us to prepare for the possibility of further legislation, legislation that would be for the purposes of refinement of Bioshield. If for some reason we get through the process and we find that short-term that is not needed, we do have a reauthorization that comes up very soon where there is another opportunity to refine the product that came out.

Our goal is to create the capability to deal with the unknown. I mean you have helped us focus on particular things that are out there and the Department of Homeland Security has a hit list and Dr. Fauci has a hit list over at NIH and there certainly is a lot of commonality in all the lists. If we are truly ahead of the curve, then we have to be designing some type of structure that addresses what is not on the list. What gives us the capabilities, the flexibilities, the assurance that when something happens, that we are at a point where everything just progresses naturally. And we have got the ability to have an answer.

I am not sure that we are there yet, and I think your testimonies today have enabled us to realize that in a very real way. I am disappointed that nobody or at least our first witnesses from HHS and DHS did not stick around. I think outside of antitrust, this is a great opportunity to hear from people who have companies and individuals within academia who really are experts on this, and I would encourage any representatives from there to make sure that those individuals have an opportunity to read the testimony, and I would encourage those agencies in the future that it is probably to everybody's benefit for witnesses to stay around. If not, we will reverse the order of the subcommittee hearing so that they are forced to stick around because I think that their interest, not just their expertise, their interest is needed if, in fact, we are all to be successful in this process.

At this time, I would ask unanimous consent that the record of this hearing remain open for 10 days as is customary on this committee so that members may have the opportunity to pose additional questions to our witnesses. Without objection so ordered. We also have written testimony of several witnesses submitted by Senator Bingaman, and without objection, it will be entered into the record.

Senator BURR. This subcommittee hearing is adjourned.

[Additional material follows.]

ADDITIONAL MATERIAL

GENERIC PHARMACEUTICAL ASSOCIATION,
February 8, 2005.

HON. RICHARD BURR,
HON. EDWARD KENNEDY,
Subcommittee on Bioterrorism and Public Health Preparedness,
Senate Health, Education, Labor, and Pensions Committee,
U.S. Senate,
Washington, D.C. 20510.

DEAR CHAIRMAN BURR AND RANKING MEMBER KENNEDY: As Congress looks for ways to better protect the population against potential biological threats, it is vital that any initiative: (1) uses appropriate financial and legal liability protection incentives to produce a novel countermeasure against known chemical or biological agents; (2) provides for rapid production and dispersal of the countermeasures; (3) spreads the costs of research and development evenly; and (4) avoids unnecessarily and excessively increasing cost to consumers, businesses, and public purchasers by providing new loopholes to block access to affordable generic drugs.

The BioShield bill that was signed into law last year was a positive first step toward finding and producing vaccines and treatments for several high-risk agents. Although the program is just getting started, there already has been a movement in Congress to expand BioShield to include additional incentives for companies to conduct research and development to manufacture a larger variety of countermeasures. While GPhA supports the concepts behind expanding research and development of novel drugs to combat the biological and chemical threats that face the world, any proposal should not needlessly delay generic competition of everyday medicines at the expense of the overstretched health care budgets of employers, consumers, and Federal and State Governments.

The Protecting America in the War on Terror Act of 2005 (S. 3) remedies some of the shortcomings of the BioShield legislation; however, it includes unnecessary patent extensions for everyday medicines that will cost consumers tens of billions of dollars by delaying generic competition. With Medicaid reform on the horizon, State health budgets shrinking, and the Medicare prescription drug program coming into effect in the coming year, the Federal Government cannot afford to further increase prescription costs by billions of dollars a year by needlessly reducing the availability of affordable medicines.

S. 3 would give a very wide variety of everyday medicines UNLIMITED patent extensions, providing brand manufacturers with huge payouts for minimal research or licensing efforts at the expense of consumers, especially seniors and the uninsured—individuals who need affordable versions of these medicines most. (Title I, Subtitle A, Chapter 1, Section 113 (c)(1)).

• S. 3 defines a countermeasure so broadly that almost every drug in most people's medicine cabinets would qualify. Commonly prescribed drugs that treat headaches, nausea, and depression would be eligible for patent extensions with minimal testing performed by the brand manufacturer. Patent extensions on these products would put the healthcare system in crisis by forcing tens of billions of dollars in expenditures on these already profitable drugs.

• S. 3 would extend the patent terms of products that qualify as countermeasures up to the full amount of time from when the patent is issued until the product is approved. Current law balances innovation and access by providing only 5 years of the regulatory review period to be added to the patent's life. If a company were given the full review time under an unlimited regulatory review period, it could add a decade of patent exclusivity and monopoly pricing per brand product. Moreover, providing patent extension for the full development time is contrary to the intent of the goal of expediting research and development.

• **S. 3 also would allow for unlimited patent extensions per product.** Under current law, only one patent can be extended for developing a novel drug product. Under S. 3, multiple patents claiming the brand drug can be extended, forcing consumers to pay monopoly prices for many years to come.

S. 3 allows for ANY patent on ANY drug product of a brand company to be extended by up to 2 years when that company has a product approved as a countermeasure. (Title I, Subtitle A, Chapter 1, Section 113 (d)(1)).

• When the company gets a countermeasure product approved (even for a secondary use to treat a common ailment, or merely licenses research from some other entity), the company is eligible to receive a "wild card" patent extension. This "wild card" in effect transfers the awarded patent extension to any other product the com-

pany makes. For example, if Pfizer were to have a countermeasure labeling statement approved for an already existing product, it could reap up to 2 extra years of patent monopoly for a blockbuster drug such as Viagra.

• And, if Pfizer decided to license a product for which another drug company performed all the requisite research and development, Pfizer could still receive yet another wild card. This time, Pfizer could decide to extend its monopoly for another one of its blockbuster drugs, or put a second wild card on Viagra.

• The result of this legislation would be an additional 2 year delay of generic competition for all major blockbuster drugs. If the "wild card" extension was only applied to the current top 20 revenue generating pharmaceuticals, it would provide tens of billions of dollars in uncontested sales for the brand manufacturer.

• Additionally, as the term implies, the "wild card" extension can be pocketed by the company and can be applied at any time before patent expiration, creating uncertainty for generic companies to invest in the requisite development of affordable medicines. Having certainty in timing as far out as possible before the patent and exclusivity periods end is what allows affordable medicines to enter the market quickly, efficiently, and inexpensively. Any added uncertainty will increase costs for all generic pharmaceuticals in the future.

While S. 3 allows for brand companies to be rewarded for the simple testing for new indications of currently marketed drugs, the Federal Government already has determined which everyday medicines are effective countermeasures for known bioterror threats.

For instance, the CDC, NIH—NIIAD and Department of Defense provide a wealth of information on currently available products to use in case of exposure to many forms of biological and chemical agents. Since the research already has been performed at taxpayers' expense, there is no reason the brand pharmaceutical company that manufactures the product should be given any additional patent life on that product or any other product.

• It would be much more efficient and cost effective for the FDA to establish an "Emergency Drug Preparedness Compendium" consisting of an approved emergency biodefense drug monograph for each drug a Federal agency (CDC, USAMRIID, NIAID, DOD, USDA, etc.) has identified as an effective agent to treat, detect or prevent harm from any biological (including an infectious disease), chemical, radiological, or nuclear agent that may cause a public health emergency affecting national security.

GPhA does support many of the ideas included in S. 3 that are needed to facilitate future development of vaccines and other treatments for bioterrorism threats. As Congress looks forward to determining the best course of action, it is important that these provisions are included in the legislation.

• S. 3 includes necessary liability protections for drug manufacturers as they develop and produce these potentially life-saving treatments. (Title I, Subtitle B, Chapters 1 and 2).

• S. 3 also includes tax incentives and manufacturing grants to companies for research and development in bioterrorism countermeasures. (Title Subtitle B, Chapter 3). As the vast majority of research is done by small biotechnology companies, these incentives are much more pertinent than patent extensions that would have little or no benefit to these companies.

• S. 3 includes fast-track approval authority for these products. Allowing FDA to speed these countermeasures to market will ensure that they are available when they are needed. (Title I, Subtitle A, Chapter 2).

The BioShield program has been a success in its short history, and any expansion of these provisions should be based on the same procurement model incorporated in that legislation.

• The upfront funding gives the research companies the resources they need at a fraction of the cost that would result from unlimited, protracted and needless patent extension provisions.

• The Federal Government already has contracted $5.6 billion in research for vaccines and treatments for the agents spelled out in the original BioShield legislation last year. Additionally, without the need for any further incentives, vaccines for smallpox, modified anthrax, and ebola are now close to being approved.

Sincerely,

KATHLEEN D. JAEGER,
President and CEO.

PREPARED STATEMENT OF RANDI AIROLA

I am a Veteran who served honorably in the Army and Air National Guard from 1991–2000. This testimony is to serve as part of the public record regarding "Biodefense Next Steps" as presented to the Subcommittee on Bioterrorism and Public Health Preparedness.

I received my first 3 doses of the anthrax vaccine in late 1998, followed by the 4th injection in March of 1999. Two days following my 4th shot I began experiencing extreme fatigue that nearly kept me bed-ridden the following week. I began noticing I would get gray-outs with overexertion. I had such severe migraines that I averaged approximately 16,000 mg. of Motrin daily. I began getting winded climbing a flight of stairs. I noticed when I bent my joints there was an audible crack; others noticed it, too. I had no strength in my arms or my legs. I forgot passwords to programs that I would use everyday. I was easily confused and found myself unable to concentrate or focus on more than one task at a time. I was easily agitated and it took everything I had to hold back on acting out physically. I was 26 years old at the time, with no history on any of the above problems preceding my 4th shot. I was seeing civilian doctors weekly who were baffled by my condition, considering I was previously in perfect health. In a 2 month time span, I missed approximately 140 hours of work, and no one in command authority found this to be a sign that there was something wrong. I had a cat scan and MRI done to check for tumors to possibly explain the migraines. It was determined that I was too young to have had a stroke, so the cause of the paralysis that would occasionally occur on the left side of my body with a cough or sneeze was left undetermined. Military doctors never examined me, nor seemed interested. When the time came to receive my 5th shot, I was still experiencing the above problems. I was denied any referral to see a competent military physician for a second opinion. As a result of my problems, for the sake of my own health, I refused my 5th shot. I was ultimately discharged from service with an honorable discharge. As a result, I also lost my civilian position as an Air Technician. I was not eligible for VA disability or compensation, as I was never classified as Active Duty.

From 1999 through 2002 I was on approximately 19 different medications for my ailments. I ultimately received help through a nutritionist; today, I am on no medications.

I am directly and intimately involved with the Military Vaccine Education Center, Inc., at www.milvacs.org, which was formed in 2004. The organization exists to provide medical and legal resources, networking, and current information to those who have been vaccinated by the military's mandatory bioterrorism vaccines. We help soldiers/veterans and their families with referrals, the process of going through Medical Evaluation Boards; the process of receiving treatment through the Vaccine Healthcare Centers, V.A. disability or compensation, etc. I have chosen to stay involved with our soldiers and the problems surrounding the anthrax biological vaccines, as I know first hand the debilitating problems that soldiers and their family can go through. It was one of the worst experiences in my life, and as long as I was and am able to, I have chosen to help others who were and are in the same shoes I was in. I have communicated with over 1,000 service members (or members of their families) who were/are having problems with the anthrax vaccine. Last year, I compiled the records of 100 individuals into a 36-page document that I sent to the Veterans' Affairs Committee. All of these individuals had reported their problems and vaccine reactions to me within a 6 month time period. No one on that committee seemed to care, as I never heard a response.

I took the initiative to learn the process of how soldiers were to get help through the Walter Reed Vaccine Healthcare Center(s), a process mandated by Congress in 2001. This information was not being passed down to the troops by the Department of Defense or by their chain of command.

With the anthrax vaccine alone, I have spoken with and met many soldiers who all had one thing in common. They were all healthy before the anthrax vaccine, and are now stuck with a life-changing ailment for a time that no one knows how long considering long-term studies have not been conducted. Some in their 20's, walk with the assistance of a cane; some cannot walk at all. Some were able to get help through the Vaccine Healthcare Centers, which at least helped them through their Medical Evaluation Board and VA compensation; others were not that fortunate.

As of now, as noted in an article in *Global Security Newswire*, "*U.S. Army Provides no Funds for Vaccine Healthcare Centers*," as quoted by Col. Renata Engler, the Walter Reed Vaccine Healthcare Center evaluated over 1,000 patients, and consulted with more than 139,000 individuals via phone/email as a result of problems with the anthrax/smallpox vaccine in 2003 alone. The Vaccine Healthcare Centers are always on the verge of losing their funding, and are overloaded with the current

anthrax and smallpox vaccine caseloads; yet more biological vaccines are being discussed and developed. Who is going to take care of those that become ill from these new vaccines, or is that not a factor? No information will be available regarding human data for safety studies, so how many soldiers will be denied admission of a causal relationship between adverse events and the vaccines?

The War on Terror has become a droning drum beat that many believe exists solely for the purpose to benefit the pharmaceutical companies and their shareholders. If protection of the soldiers or the American people were actually the focus, then better detection and outer protective equipment would be the primary goal. It stands to reason that if an enemy knows a vaccine exists for a specific strain of biological warfare, a genetic alteration of that strain would render that vaccine useless. Where is the logic of spending billions of dollars on biopreparedness through vaccinations, where the only thing that is at least known is that it can become easily obsolete?

Who will regulate the use of these vaccines?

- The DOD? The agency that can't even comply with a Federal Judge's order or Congress?
  - Vaccinations were given despite Judges Order; http://www.washingtonpost.com/wp-dyn/articles/A59190-2005Feb2.html?sub=AR
  - "*DOD's medical credibility disputed*" http://www.govexec.com/dailyfed/0200/020100b3.htm
  - "*Army Proposal to use U.S. Soldiers as Human Test Subjects*;" (http://www.bna.com/press/guest/aotto.htm).
  - "*U.S. Army Buys $30 Million in Anthrax Shots*" (http://dailynews.att.net/cgi-bin/news?e=pri&dt=040102&cat=news&st=newshealthan). [1]
- The FDA? As best put by David Graham in his testimony before a Senate hearing:
  - "This culture [at the FDA] views the pharmaceutical industry it is supposed to regulate as its client. It overvalues the benefits of the drugs it approves, and seriously undervalues, disregards and disrespects drug safety."
  - "The FDA, as presently configured, is incapable of protecting Americans against another Vioxx."
- The NIH? The agency that has recently come under fire for its conflict of interest with the drug manufacturers?
  - "*Panel Wants Top Health Officials Off Drug Payrolls*," (http://www.ahrp.org/infomail/04/05/07.php).
  - "*NIH to Ban Deals with Drug Firms*" (http://www.latimes.com/news/nationworld/nation/la-na-nih1feb01%2C0%2C5059199.story?coll=la-home-headlines). [2]

The regulating agencies have become such a revolving door, it's hard to determine where one agency ends and the drug manufacturer's door begins. Though NIH is taking steps to correct the conflict of interest, the fact that such a move even needs to occur should sound major alarms. The public is becoming extremely wary of these regulating agencies. People within these agencies have lost sight of their primary responsibility to the public, unable to see beyond their own greed.

I'd like to remind the committee of the Government's own words on vaccination biological programs:

- "*House Democrats Call for Revitalizing U.S. Smallpox Vaccine Program*" (http://www.nti.org/d_newswire/issues/2004_1_29.html#88E92E9A). [3]

---

[1] The Defense Department announced on Friday a $29.7 million order for anthrax vaccine based on the assumption that a Federal judge's ban on mandatory inoculations will be served.

[2] For the last decade, government scientists at the NIH have quietly been allowed to consult for biomedical companies under policies that defenders have said helped attract talented personnel to the agency. Hundreds of scientists took millions of dollars in fees and stock from industry. Most of the payments were hidden from public view, raising questions about the scientists' impartiality in overseeing clinical trials and in making recommendations to doctors for treating patients. In some cases, NIH scientists worked for drug companies that directly benefited from their recommendations to doctors. In other cases, scientists appeared at public forums and commented upon or endorsed treatments or drugs without revealing that they were on the payroll of companies making the products.

[3] Calling Federal efforts to vaccinate U.S. health care workers against smallpox "an embarrassing failure of government, with serious implications for homeland security," Democracts in the U.S. House of Representatives yesterday called on the Bush administration to reassess the smallpox bioterrorist threat and improve the U.S. ability to respond to such an attack.

• *Study Slams Biodefense Plan* (http://www.boston.com/news/nation/articles/2004/01/23/study_slams_biodefense_plan/).[4]

We do not know the final outcome of the current vaccines in use, let alone any new ones that are yet to come. So far, what is known is that the anthrax vaccine has been linked to birth defects, spontaneous miscarriages, auto-immune disorders, which include (but are not limited to): Bell's palsy; Guillain Barre Syndrome; Multiple Sclerosis; Lupus and heart disease.

(http://www.fayettevillenc.com/printer.php?Story=6787445).[5]

Taken directly from the product label, further associations to the anthrax vaccine, to also include death, are as follows:

"Other infrequently reported serious adverse events that have occurred in persons who have received BioThrax have included: cellulitis, cysts, pemphigus vulgaris, endocarditis, sepsis, angioedema and other hypersensitivity reactions, asthma, aplastic anemia, neutropenia, idiopathic thrombocytopenia purpura, lymphoma, leukemia, collagen vascular disease, systemic lupus erythematosus, multiple sclerosis, polyarteritis nodosa, inflammatory arthritis, transverse myelitis, Guillain-Barre Syndrome, immune deficiency, seizure, mental status changes, psychiatric disorders, tremors, cerebrovascular accident (CVA), facial palsy, hearing and visual disorders, aseptic meningitis, encephalitis, myocarditis, cardiomyopathy, atrial fibrillation, syncope, glomerulonephritis, renal failure, spontaneous abortion and liver abscess. Infrequent reports were also received of multisystem disorders defined as chronic symptoms involving at least two of the following three categories: fatigue, mood-cognition, musculoskeletal system.

Reports of fatalities included sudden cardiac arrest (2), myocardial infarction with polyarteritis nodosa (1), aplastic anemia (1), suicide (1) and central nervous system (CNS) lymphoma (1). (http://www.bioportcorp.com/AnthraxVaccine/insert/avainsert.asp).

According to Ron Brookmeyer, a professor of biostatistics at Johns Hopkins Bloomberg School of Public Health, mass vaccination programs aimed at protecting most or all Americans against anthrax are impractical and would save fewer lives than a speedy, localized response in the event of an attack, a new report concludes.[6]

The smallpox vaccine has been linked to enough heart problems that the civilian program for first responders was put to a halt; yet it's still mandatory for our military personnel.[7]

Further vaccinations that are in the talking/planning stage to be tested on our soldiers should be used only with informed consent. Any forced vaccinations on our troops would make the U.S. Government solely responsible for any and all negative outcomes regarding adverse events, which will inevitably occur. Has the committee considered how many negative adverse events or deaths from these vaccines will be considered an acceptable loss? According to President Bush's State of the Union Address on February 2, 2005, "the destruction of life is not acceptable for medical research." It takes 5 to 7 years after approval before a new drug's risks are fully understood. Do these biological vaccination programs not stand in complete contrast to the President's own words?

It is the members of our Armed Forces that will be forced to test these vaccinations, with no option of refusing, no recourse to take should they become ill and lose their health and career; yet talk continues about shielding the manufacturer's from liability should these events occur—what about our service members? Where is their shielding? Pure rhetoric rallies support for our troops from the legislature at elec-

---

[4] The Pentagon's efforts at creating new vaccines and drugs to combat biological weapons are poorly organized, under-funded, and unlikely to produce successful results in the near term, if ever, according to a congressionally mandated study released yesterday.

[5] Tech. Sgt. Lavester Brown almost died last year when his heart swelled to twice normal size hours after he received an anthrax vaccination. A few months later, he had to have a heart transplant.

[6] http://www.forbes.com/lifestyle/health/feeds/hscout/2004/12/15/hscout522909.html.

[7] Lexis-Nexis—Friday September 3, 2004—Vaccine-induced heart problems; Smallpox vaccinations and anthrax vaccine—Smallpox vaccinations have been linked to serious heart problems. Seventy-seven of over 615,000 (1.25 percent), according to the Pentagon, have developed myopericarditis, an inflammation of the sac around the heart. The Centers for Disease Control say that 21 of the 39,500 (5.3 percent) U.S. medical professionals who received the vaccination also contracted the illness. When three people enrolled in clinical trials to test a new smallpox vaccine, developed by British biotechnology company Acambis, also developed myopericarditis, the company ended the trial. The anthrax vaccine, which is also linked to heart attacks and strokes, is being implicated in unexplained blood clot disorders, according to a report by United Press International (October 6, 2003). The label on the anthrax vaccine given to military personnel "warns of infrequent reports of heart attacks or strokes." Both can be caused by blood clots. Several soldiers and an NBC news correspondent have suffered—and in some cases died—because of unexplained blood clots.

tion time, or the beginning of wars, yet falls short when it comes time to put actions behind the words. Our military has given our Nation their all; should they at least not be given some of their God-given rights: The right to have integrity over their own bodies?

The continuous rotation of deployment of our troops in Afghanistan and Iraq with the War on Terrorism, has caused a major strain on our forces. Further requirements of biological vaccinations with unknown risk factors will break an already thin force.[8]

"*Dover short pilots since vaccine order*" (http://www.delawareonline.com/newsjournal/local/2004/12/28dovershortpilot.html).

The men and women who serve in our military may not be your sons or daughters, but they are someone's. As you think about the "Next Steps in Biopreparedness," please keep that in mind. Until then, my colleagues and I will continue to assist the soldiers and their families the best we can—those whose lives have already been destroyed, by just two of these biological vaccines.

The Government continues to try and find ways to combat terrorism and biological warfare. Aggressive measures should be taken; however, we need an honest and open assessment from all parties concerned regarding biopreparedness and the next steps, which goes beyond pharmaceutical companies and the NIH. Our Nation is billions of dollars in debt, and spending billions of more dollars on biological vaccination programs that may fail on all counts, is financially and morally irresponsible. I submit my testimony today not as an expert in biowarfare, but, as a concerned individual that has seen, in some cases, the deadly and life-changing result that has occurred from biological vaccines.

I am a volunteer, and I do this willingly along with my colleagues, considering we care more about our troops than the Department of Defense or most of those in the legislature. Perhaps when the members of Congress have to begin getting intimately involved in receiving these vaccinations, or enlisting their sons and daughters into the Armed Forces, they may finally realize that those receiving these vaccines are, in fact, human beings, not dispensable models. Perhaps then, Congress will begin to provide the civilian oversight of the Department of Defense as it is supposed to do. Perhaps then, the Department of Defense can get back under control; and perhaps then, soldiers will once again begin to display faith in their leadership.

In closing, I am willing, at any time, to speak with anyone concerning any questions you may have. My email address is: randi@milvacs.org; my phone number is 517–819–5926. Thank you for the opportunity to submit this written testimony for public record.

STATEMENT OF MERYL NASS, M.D.

Thank you for the opportunity to submit this testimony for the record. My name is Meryl Nass, M.D., and I have worked for the past 20 years as an emergency physician and internist in community hospitals. I have also studied many aspects of bioterrorism since 1989. I am the person who first demonstrated that one could investigate an epidemic retrospectively, and prove that it was due to biological warfare, using Rhodesia's 1978–1980 anthrax epidemic as a model.[1]

Since then I have authored and coauthored numerous documents on the subjects of preventing, investigating and ameliorating the effects of a bioterror attack. These included recommendations to the Biological Weapons Convention Review Conference of 1996,[2] and a Congressional testimony on medical responses to bioterrorism in November 2001.[3]

Because I continue to practice medicine, have a strong background in biological warfare, and do not consult for the drug industry, my concerns may differ from most Congressional witnesses. They are:

(1) Achieve maximal readiness at the local level.

(2) Assure the development and availability of safe and effective measures, especially drugs and vaccines, to protect our citizens.

---

[8] When the military ordered all military personnel bound for Korea and the Middle East to be inoculated with the anthrax vaccine, pilots staged a massive walkout at Dover Air Force Base, where the Air Force's largest cargo aircraft are flown.

[1] Nass M. Anthrax Epizootic in Zimbabwe 1978-1980: Due to Deliberate Spread? PSR Quarterly, 1992; 2: 198–209. http://www.anthraxvaccine.org/zimbabwe.html.

[2] Report of the Subgroup on Investigation of Alleged Use or Release of Biological or Toxin Weapons Agents. Federation of American Scientists Working Group on Biological Weapons Verification, April 1996.

[3] Preparing a Medical Response to Bioterrorism. Written Testimony of Meryl Nass, M.D. House Committee on Government Reform hearing, November 14, 2001: Comprehensive Medical Care for Bioterrorism Exposure.

(3) Urge a much stronger focus on prevention of bioterrorism. Although it is a truism that it is impossible to fully protect our population against this form of attack, in our rush to buy protections we seem to ignore their limitations. The ability of an enemy to defeat our preparations will increase in the future. Furthermore, the potential for biowarfare to destroy whole species or even end life as we know it is not inconsiderable.

I'd like to briefly cover these three issues. With respect to local readiness:

Through State and Federal grants, hospitals have been given antidotes for chemical agents, and other appropriate drugs for use in a limited chemical or bioterrorism event. Hospitals do not have sufficient stockpiles of these substances to care for more than a tiny percentage of the population, should a massive event occur. We have even fewer people with the knowledge or experience to take charge of the situation appropriately, should a terrorism event occur. We lack sufficient gloves, gowns and masks on site in the hospital to handle a sustained infectious catastrophe.

Our practice and knowledge of infection control needs to be improved. During the past month my hospital had several cases of hospital-acquired influenza in both staff and patients, despite following CDC-specified infection control measures. This occurred, in my opinion, because CDC did not pay adequate attention to transmission of the virus by fomites (inanimate objects that harbored transmissible virus) and because we had patients who were spreading virus prior to being diagnosed with the infection, i.e., before appropriate control measures were instituted, because it took up to 24 hours to get lab confirmation of the diagnosis. As most of the flu cases I cared for had received flu vaccine, flu was not suspected initially. Yet the vaccine apparently failed to protect them.

Attention to improving our understanding of infectious disease management will yield great dividends in helping us control a bioterrorism event. I am simply repeating what many others have said: the public health system has been a poor stepchild of the medical system for decades, generally relegated to providing a modicum of care for those who cannot pay, and handling conditions like tuberculosis and sexually transmitted diseases. It needs to expand its horizons, and it should become fully integrated into our practice of medicine.

My second concern is that the provision of safe and effective drugs and vaccines to our population is of utmost importance. However, we cannot develop and manufacture a vaccine or antidote for every possible infectious agent for compelling reasons:

(a) we do not yet know how to do so (witness the lack of an AIDS vaccine or an effective drug for viral hepatitis).

(b) the number and variety of potential pathogens is infinite, so we cannot predict or identify all the pathogens that might be used as weapons, which makes finding treatments difficult or impossible.

(c) the cost of developing and producing even one drug or vaccine for the entire population is likely to range from one to many billion dollars.

At this point, the United States has not even begun to develop a surge capacity for manufacturing such products, although it is clear this is what is required. My 2001 Congressional testimony included many suggestions for rapid development of effective drugs and vaccines, so I will not belabor those points today.

What is urgently needed by the Nation is for a group of knowledgeable, nonpartisan experts in and out of government to review our weaknesses and strengths, and plan an overall approach to the problem of bioterrorism, while avoiding measures that could increase the threat. Until now, we have put the cart before the horse, purchasing a few drugs and vaccines (that may in fact be unusable due to problems that are only now being identified), without any overall program to protect the Nation from the range of threats we face. Instead, there has been great duplication of efforts by agencies with overlapping responsibilities, but little attention to systematically plugging the gaps in our preparedness.

NIAID was given a large amount of money in 2002 to allocate to bioterrorism preparedness, and elected to use much of it to support building new high containment laboratories around the country. Although some additional capacity was probably needed, much of the additional capacity appears at this stage to be superfluous. More worrisome than wasteful, however, is the fact that the new labs will employ thousands of scientists with new careers in bioterrorism, who will study weaponizable pathogens, thus proliferating knowledge about these pathogens. This could lend itself to serious blowback in the future. We have no systematic mechanisms in the civilian sector to screen these scientists and other new biodefense employees, nor have we the means to prevent researchers from taking miniscule samples of pathogens out of the lab, nor to follow their activities once they leave our research centers. Nor do we have foolproof systems to maintain the security and safety of the labs. An electrical failure with loss of generator capacity at Plum Is-

land, New York 2 years ago graphically demonstrated that even redundant systems can fail, and that one may not always be able to keep dangerous pathogens safety confined. It is simply not possible to have a fail-safe system. Researchers can become infected and bring their illness to the community; cultures thought to be dead or attenuated are found to be virulent.

Plum Island was chosen for biodefense work decades ago because there was no land link to Long Island or the U.S. mainland. This was a powerful safety measure that we are now ignoring at our peril. There cannot be a sufficient rationale for siting biodefense laboratories in heavily populated areas, even if this makes attracting quality staff easier. The hubris of assuming that nothing can go wrong does not augur well for the scrupulous safety planning that should be taking place, particularly in light of accidents at these very same labs in the recent past. (Three researchers at Boston Medical Center developed tularemia and one researcher at Fort Detrick developed glanders recently as a result of working with the organisms; in each case, it was not suspected until late that they were ill due to occupational exposures).

How do we best get safe new drugs and vaccines to the population? I would venture to say that when government has employed medical therapies for political ends, rather than for a demonstrated medical need, the strategy often backfires. Using public relations techniques to create a need for treatment in the public's mind is another dangerous strategy with a tendency to backfire, as the public learns to mistrust the medical pronouncements of government. This probably accounts for why we have a flu vaccine surplus today, despite what was touted as a dangerous shortage several weeks ago.

The swine flu vaccine program of 30 years ago failed because vaccine was made and Americans vaccinated due to a political program, in the absence of an outbreak. In order to get rapid production of vaccine by industry, the Federal Government assumed the liability for vaccine-induced injuries, and paid for many cases of neurological illness. Americans learned that Guillain-Barre Syndrome could be caused by vaccines.

In 1998 the anthrax vaccine was rolled out as the first immunization in a potentially large program of vaccinations to protect the military from biowarfare threats. Here again the Federal Government, in the person of the Secretary of the Army, indemnified the manufacturer against all liability from adverse effects or product failure. This measure was reportedly designed to avoid costs, but may become quite costly, due to ongoing litigation about the vaccine's safety and efficacy. The vaccine's license for prevention of inhalation anthrax was removed in October 2004 by Judge Emmet Sullivan.

The ability to shift the costs of product indemnification by Federal agencies probably works to make indemnification attractive. Although it was the Army that indemnified the vaccine manufacturer (reducing the manufacturer's need to produce a quality product) soldiers who become disabled as a consequence of anthrax vaccination are paid primarily by the Department of Veterans Affairs and/or Social Security Disability. So far there has been little impact on the Army's budget from its decision to use a poorly tested and manufactured vaccine.

In late 2002 the Federal Government initiated the smallpox immunization program, with plans to vaccinate, stepwise, 10 million first responders and medical personnel. The manufacturer, Wyeth, had turned over its smallpox vaccine stockpile to the Federal Government 2 decades ago, and it too received immunity from liability claims. Due to a poor initial response by volunteers, Congress crafted a plan to insure vaccine recipients against death or disability, with a maximum payout per recipient of $262,100. However, despite this guarantee, higher than expected rates of cardiac complications caused the pool of volunteers to dry up. The civilian smallpox vaccine program withered on the vine in late 2003, but mandatory military smallpox vaccinations have continued, perhaps helped along by shifting the costs of the programs's adverse medical consequences to other agencies.

In November 2004, FDA added a black box warning to the vaccine label, limiting use to only those at high risk of smallpox, and indicating that myocarditis was occurring approximately 100 times more often than initially reported: one in every 145 vaccine recipients had developed this complication in a clinical trial conducted by industry. The military smallpox program continued nonetheless.

A historical lesson that industry may not want to acknowledge is that when the removal of manufacturers' liability is sought and obtained, the resulting products have usually been associated with serious safety issues. And when the government assumes the liability, it has a strong disincentive to perform appropriate scientific studies that will identify and quantify the health risks of such products. Thus we still lack reliable statistical data on the types and rates of adverse reactions for anthrax vaccine. And despite CDC surveillance of 40,000 smallpox vaccine recipients,

we remain in the dark about the rates of vaccine complications, apart from myocarditis and skin conditions.

The Food and Drug Administration used to be the preeminent agency in the world for protecting citizens from bad drugs. Unfortunately, this began to change about 10 years ago, spurred by two Congressional-FDA initiatives: the Food and Drug Administration Modernization Act and the Prescription Drug User Fee Act.

Encouraged by the Executive branch, FDA came to view industry as its primary client, rather than the public, and focused more on rapid drug approvals than on assuring safety and efficacy of new products. Allowing direct-to-consumer advertising further damaged the agency's reputation. This also made it harder for physicians to prescribe medicines cost-effectively. Ignoring serious bacterial contamination in 2004 at flu vaccine manufacturer Chiron Corporation, FDA demonstrated a willful failure to carry out its responsibility for assuring good manufacturing practices.

Things have gone from bad to worse at FDA lately. The large number of recent drug withdrawals, the continuing series of scandals involving FDA's connivance with industry to hide serious adverse drug effects, and widespread loss of trust—by its own employees—that the FDA can do its assigned job grace the pages of our newspapers daily. The fact that the American Medical Association recently recommended that assessment of drug safety be performed by a separate agency confirms that the credibility of FDA has dropped to a critical level, and serious reforms are way overdue.

It is this flawed, unreliable FDA that is now charged with approving new drugs and vaccines for bioterrorism: products likely to receive less testing, using fast-track procedures, than for standard drug approvals. This FDA also approves the use of *unlicensed*, investigational products under certain circumstances, and has just done so for the military with anthrax vaccine.

Given FDA's ongoing credibility problems, the procedures currently in place to assure that American citizens obtain safe and effective products to prevent and treat diseases due to bioterrorism are inadequate. We are talking, after all, about drugs that cannot be tested for efficacy in humans: potentially the entire Nation could receive such drugs or vaccines that have had only rudimentary human testing. And animal testing is uniformly acknowledged to be inadequate to assess human safety.

Americans cannot currently rely on FDA to guarantee quality manufacturing, testing, safety and effectiveness of these products. Because these drugs are likely to be used all at once, i.e., the entire Nation might be treated during the same week, we will have only very limited information about the drugs' side effects and effectiveness when the decision to use them is made. We will not have acquired the clinical familiarity and longer term data that accrue over the 1st year or 2 of a new drug's use, and upon which most physicians rely.

As a clinician, I consider this entirely unacceptable. Such drugs need more attentive oversight than ordinary drugs, not less, before they are approved for use. A reliable track record must exist before I can prescribe a drug or vaccine. Because all drugs cause adverse reactions in some recipients, and the administration of every drug involves a risk-benefit calculation, their appropriate use requires care and skill. No one should decide to prescribe for the Nation without the availability of reliable information on the drug to be used. Yet current law permits the Secretary of HHS to do so, even if that person has no medical training. He may consult with the FDA Commissioner; but the current Acting Commissioner is a veterinarian. HHS will bear no financial liability if the drug turns out to be more dangerous than anticipated.

Of course industry needs incentives in order to develop and produce useful products. I submit that current patent protections for industry should be changed. Why should the clock start ticking on a drug patent the day the patent is issued, even though this is years before FDA approval is obtained and the product can be manufactured? The ticking clock forces FDA to eschew safety considerations for speed.

A preferable alternative would be, for example, to extend patent protection based on the date of FDA licensure. This would give FDA and the manufacturer breathing space, allow for clinical safety trials of longer duration, and give the manufacturers a reasonable incentive. In order to speed new drug development, the length of patent extension could also become a function of how quickly the new product is developed. Another advantage to this proposal is that it would remove the incentive manufacturers now have to rush out drugs before they are well understood.

Other incentives for industry have been discussed elsewhere, but should not be used if they are associated with significant safety risks. Industry may wish to use certain products, such as currently unlicensed vaccine adjuvants, in vaccines designed for bioterrorism because they improve efficacy. Possibly this back door approach would help them move these adjuvants toward licensure. However, given the

known risk of these products to induce autoimmune disorders in susceptible recipients, bioterrorism must not become the excuse to initiate their widespread use in humans.

My final point is that prevention of bioterrorism should be the top priority of Bioshield legislation. Because we cannot afford to protect against all potential pathogens, because we cannot even predict the potential pathogens we might face, and because the minute size of microorganisms makes bioagent proliferation extremely easy, it should be clear to all that we will never be able to purchase adequate protection from bioterrorism, no matter how many resources we expend. Therefore, finding ways to maximize international cooperation in the development of countermeasures, in inspections of biological research and manufacturing facilities, and in preventing the proliferation of bioweapons scientists should receive our full attention and resources.

It is hard to understand why successive U.S. administrations have failed to embrace the value of this approach, and why diplomatic measures, such as strengthening the verification provisions of the Biological Weapons Convention, have not received strong support from the U.S. government. This is a low cost approach that can be undertaken in tandem with all the other measures designed to boost protection for our population. Although industry had reservations about inspections in the past, because of the potential loss of trade secrets, PHaRMA now supports strengthening the Biological Weapons Convention with inspections and other efforts.

The clock is ticking for our species and planet. We can throw money scattershot at this problem and move on, or we can give it the prolonged attention and effort it deserves, and ask some of our strongest scientists, engineers, and statesmen to help think through the overall problem of readiness and appropriate preparation. If we are to take the threat seriously, we must maximize our resources on the local and global levels. So far we have not done so. Thank you.

THE MILITARY VACCINE EDUCATION CENTER,
MISSOULA, MT 59807,
February 7, 2005.

Hon. JEFF BINGAMAN,
Subcommittee on Bioterrorism and Public Health Preparedness,
U.S. Senate,
Washington, D.C. 20510.

RE: Feb. 8, 2005 Hearing on Biodefense: The Next Steps

TO MEMBERS OF THE COMMITTEE: My name is Kathryn Hubbell, and I am writing as President of both the Military Vaccine Education Center, Inc. (www.milvacs.org), a networking, resource and referral center for troops and veterans, and the Military Vaccine Action Committee, L.L.C., a "non-connected PAC" (www.mvacpac.org).

I am hoping these remarks and the accompanying timeline will prompt you to learn from the mistakes—the outright disasters—that have occurred with the military's mandatory bioterrorism vaccines, so that as you move forward discussing ways to help the public, these same mistakes will be replaced by sound policy, medically stringent procedures, and proper protocol.

I am very tempted to relate to you the heartbreaking letters we receive on a daily basis from service members and veterans, describing their extreme illnesses as a result of the anthrax vaccine (and now of the smallpox vaccine); the way they are insulted and humiliated by their chains of command, who have been taught that there is no relation between these illnesses and the vaccines; their years of struggle to obtain any kind of medical benefits, a struggle which too often results in the loss of their homes, cars, jobs and marriages; and finally, their ensuing struggle to maintain a sense of dignity in the face of extreme disability, and to have faith that they still have something to contribute to their country.

But let's not go there. Many of the ill have already written to you, and you might be tempted to think "This is terrible, but these are isolated incidents."

So I would like to speak in a different language, one that looks at the larger picture and does not dwell on individual sadness. I would like to talk about numbers, processes, and finances; and finally, about alternative solutions, solutions which are badly needed because what's been done up until now for our troops has backfired badly. We should review the past steps and ask pertinent questions in order to determine what the next steps are.

Here are some facts and concepts which need serious questioning:

• The anthrax vaccine label itself—mandated by the FDA in 2002—admits to a systemic averse reaction rate of between 5 percent and 35 percent—where pre-

viously, the DOD claimed it was a mere .02 percent (http://www.bioportcorp.com/AnthraxVaccine/insert/avainsert.asp). Since then, the GAO (Government Accounting Office) has come out with a new report estimating the systemic adverse reaction rate is probably as high as 85 percent.[1] In addition, it is known that women have a much greater adverse reaction rate than men.[2]

Questions: Why would the Department of Defense risk losing over a third of its troop strength to this highly reactive, questionable vaccine?

Are we not to believe that our troops are stretched quite thin all over the world?

How many of our fine men and women in uniform have left the service because of the anthrax vaccine? This is more of a rhetorical question, because many service members leaving active duty simply didn't give the real reason. My son was one of them. He still misses the Air Force; but he misses his full health even more.

• We've had nearly 1,600 service members killed in Iraq, and several thousand have returned home wounded. *But nearly 17,000 have been medically evacuated out of Iraq due to non-combat causes.*[3]

Is this a normal figure in time of war? Is it acceptable? And exactly what are those non-combat causes? Who has the records?

How much is it costing the VA and the Vaccine Health Care Centers to treat these sick troops? Is it cost-effective to wait until they get sick and are medical-boarded out of the service, rather than provide them with protective gear and antibiotics so they can stay in and serve their country as they so much want to do?

• The 2002 GAO also stated that of the Guard and Reserve units forced to take the vaccine, at least 18 percent of the pilots resigned or obtained transfers out of their units rather than take the vaccine and jeopardize their civilian flying careers.[4]

Questions: How much does it cost to train an F-16 pilot?

How much does it cost to replace a fighter jet if the pilot suddenly suffers an attack of vertigo—one of the most common anthrax vaccine reactions—and has to bail out?

How many pilots are we short right now?

• Walter Reed Vaccine Healthcare Center saw over 1,000 patients and consulted with more than 139,000 individuals via phone/email as a result of problems with the anthrax/smallpox vaccine in *2003* alone.[5]

Questions: Why is funding for the Walter Reed Vaccine Healthcare Center constantly jeopardized?

How will we fund the four new Vaccine Healthcare Centers that are needed and proposed, when we can barely take care of the ones we've got?

If there is no connection between these illnesses and the anthrax and smallpox vaccines, why are the current Vaccine Healthcare Centers needed at all—let alone requesting expansion into other cities and States?

• The anthrax vaccine was never licensed for use against aerosolized anthrax. Despite the FDA's "finalizing the rule" for the anthrax vaccine in December of 2003, just 8 days after Judge Emmett Sullivan declared it illegal, the Vaccine in its current form *was never meant to be used against aerosolized anthrax*.[6]

Question: The FDA and the pharmaceutical industry are currently under intense scrutiny—and facing lawsuits—for drugs freely used off-label, and/or drugs whose dangers were known, such as Vioxx, but reached the open market, for years anyway. There are now consequences to pay for both Merck, the manufacturer of Vioxx, and the FDA.

If these standards and consequences are good for our civilians, why do we not uphold such standards for our troops? Are they somehow made of totally different genetic material than the families from which they came?

• The anthrax vaccine was originally licensed based on data from a different vaccine. The only safety/efficacy study ever done on human beings was done on that different vaccine.[7]

---

[1] Government Accounting Office; 2002; Anthrax Vaccine: GAO's survey of Guard and Reserve Pilots and Aircrew; GAO-22-445, p.22.

[2] Ibid. p.9.

[3] United Press International, 2004: Pentagon not listing 17,000 war casualties. (http://www.washtimes.com/upi-breaking/20040915-052239-8792r.htm).

[4] Government Accounting Office; 2002; Anthrax Vaccine: GAO's survey of Guard and Reserve Pilots and Aircrew; GAO-22-445, p.9.

[5] Rupple, David; 2004; U.S. Army Provides No Funds for Vaccine Care Centers; Global Security Newswire, May 18, 2004; (http://nti.org/d%5Fnewswire/issues/2004/5/18/b047b91a%2Dbaae%2D4469%2Da369%2Dce894037d5a1.html).

[6] Rempfer, T; Dingle, R.; Connecticut Air National Guard, 2001 An analysis of the flawed process behind the development of the anthrax vaccine, pp.1–2.

[7] Ibid.

The FDA and DOD have also previously admitted that efficacy based on animal studies against inhalation is problematic because no proven correlate of immunity between animals and humans exists for anthrax infection.

Question: Again, why are standards lowered for our troops? Why are the normal safety standards and protocols consistently bypassed when it comes to our troops?

• The anthrax vaccine protocol originally called for 3 shots only; the change to a series of 6 shots with annual boosters was done with no foundation in research or fact. The label was actually changed to reflect the protocol then in practice; the protocol was not dictated by instructions on the label. In 1985, a review panel "also found the dosage of the anthrax vaccine to be incorrect, and recommended a correction to the labeling to only 3 shots."[8]

Question: Why is it that no one went back to the source documents to understand what really happened? The problem is that the "sound bites" and convenient answers get repeated so often that they are finally accepted as the truth.

• There have been no long-term studies done of reactions to the anthrax vaccine.[9]

The bottom-line question for all of the points we have just brought up is this: Why have such shoddy processes and practices been allowed? Where were the standards for the development process and the follow-up? Why has the FDA not enforced its own rules and procedures?

• "Researchers at Johns Hopkins University said Wednesday that early detection—and not a pre-exposure vaccination—is the key to limiting an outbreak of anthrax." (http://www.cnn.com/2004/HEALTH/12/15/anthraxdetect/) Dec. 14, 2004.

• There are a number of anthrax early-detection kits and products on the market. (example: http://osborn-scientific.com/PDF/anth_data_OSG_0411.pdf). In addition, antibiotics and protective garments, masks and filters are readily available.

Question: Why are funds being directed at vaccine instead of being used for better detection equipment and better protective gear for our troops?

• The military has a tendency to administer multiple vaccines in one day—smallpox, anthrax, the Hepatitus B, and more. Nearly 2 years ago, a young Army Reservist named Rachel Lacy died within a month of receiving this assault upon her immune system.[10]

Questions: Why are non-medical commanders in charge of administering this program, instead of military physicians? Is there no one in the military medical establishment who understands that the human body cannot accommodate such an assault without severe problems?

Here's the bottom line: **If the anthrax vaccine was a civilian vaccine, it would have been pulled from the market years ago, and the resulting lawsuits would have bankrupted the manufacturer.**

We do not want to see these travesties perpetuated on the general public. At the same time, we know that it is only when the public is subjected to the same investigational drugs that a public outcry will finally force accountability over these issues.

My understanding is that you are a subcommittee dealing with bioterrorism issues and with public health. If you want to protect the public, do not treat them the way our service members have been treated. Our men and women in the military have long served as unwitting medical guinea pigs.[11]

Vaccines, at their best, still carry a risk for a certain percentage of the population. As we move into an era of more—and more difficult—bioterrorism vaccines, the terrible lessons of the past must guide our actions. We cannot afford to decimate our military due to unproven, unsafe, investigational new drugs. Nor will the general public stand for such results.

Please consider the following:

1. Demand a full explanation of the exact anthrax threat that constitutes the "emergency" recently declared by Tommy Thompson of Health & Human Services.

2. If the public is definitely facing an anthrax threat, then the triple-pronged approach—better detection equipment, antibiotics and protective clothing—is the one increasingly recommended.

---

[8] Rempfer, T; Dingle, R.; Connecticut Air National Guard, 2001: Time Line: Development and use of the Anthrax Vaccine and the Anthrax Vaccine Immunization Program.

[9] Chan, K.C., 1999; Summary of GAO's findings on the safety and efficacy of the anthrax vaccine. Letter to Hon. Steve Buyer. Government Accounting Office, NSAID-00-54R.

[10] Dept. of Defense, 2003; Panel Issues Report on Vaccine Adverse Event Case. (http://www.anthrax.osd.mil/media/pdf/safetypanelQA.pdfhttp://www.anthrax.osd.mil/media/pdf/safetypanelQA.pdf).

[11] Committee on Veterans' Affairs, 1994: Is Military Research Hazardous To Veterans' Health? Lessons Spanning Half A Century. U.S. Congress. (http://www.datafilter.com/mc/militaryHumanExperimentationReport94.html).

3. If the public genuinely needs an anthrax vaccine, or a smallpox vaccine—or a vaccine against ricin or anything else—then a new vaccine must be developed that adheres to the strictest of sound scientific and medical principles and processes. Because it takes years to run clinical trials, people must be given informed consent documents, as they were after the 9/11 attacks—the same documents our troops have never been given, but to which they are constitutionally entitled.

4. If new smallpox and other bioterrorism vaccines are going to be made available to members of our armed forces as well as civilians, there must be a better protocol in place for administering these vaccines. Giving a person multiple shots in one day is against every form of medical protocol for vaccinations that there is.

5. We are against providing complete legal protection for those manufacturing these vaccines, because we have seen what it has done to members of the armed services. They have no recourse to sue for their injuries and illnesses due to a 1950 body of law called the Feres Doctrine.[12] We are convinced that Feres Doctrine was not meant to pave the way for unregulated medical experimentation upon members of the armed services—but despite its good intent, that's exactly the result. We need to be able to hold vaccine manufacturers as well as the FDA completely accountable for the policies and procedures by which these vaccines are developed and come to market. Giving them complete immunity merely because vaccines are not a high profit-producing area for a pharmaceutical company will result in the same sloppy procedures, carelessness, haste, and desire to improve the bottom line that we have seen in the development and administration of the anthrax vaccine.

If you doubt this, consider that Vioxx was legally approved for placement on the market by the FDA. Consider that Merck had warnings about the dangers of Vioxx as early as 1996, and was able to market the drug anyway; in fact, the FDA apparently pressured a researcher to withhold evidence about the drug's dangers.[13]

All this was done working with our current system of regulation by the FDA, and with our current system of supposedly holding drug manufacturers accountable. The bottom line for Merck was that Vioxx accounted for over 10 percent of its gross earnings each year, a $2.5 **billion** dollar product.[14] It's far too tempting, given those figures, to ignore or hide warnings and proceed toward depositing that check in the bank.

Vaccine manufacturers and health care providers want protection without accountability or at best with very limited accountability—except in case of violating standard medical procedures when administering the vaccine, or in cases of gross negligence.

But, as you have just seen, the military has consistently violated standard medical procedures when administering the anthrax vaccine, and, in conjunction with the FDA, has shown gross negligence in development of the anthrax vaccine.

6. Although we are reluctant to suggest yet more government bureaucracy, we are convinced that a separate body might provide more stringent oversight of the procedures for developing and administering vaccines than does the FDA. We need an independent body that is not so closely aligned with the pharmaceutical industry, and is not beholden to the industry in any way.

Finally, I have taken the rather extraordinary step of attaching a full timeline, documented with footnotes and references, describing the flawed, careless and deceitful development of the anthrax vaccine, a process in which the Department of Defense, BioPort, Inc., and the FDA all took part. If the vaccines we want to manufacture in the future cannot be done in any better way than this, our country is in serious trouble. I thank you for your time.

Sincerely,

KATHRYN D. HUBBELL,
President, Military Vaccine Education Center, Inc.,
President, Military Vaccine Action Committee, L.L.C.

Attachment: Time Line: Development and use of the Anthrax Vaccine and the Anthrax Vaccine Immunization Program, Compiled by Major Thomas Rempfer and Lt. Col. Russell Dingle, Connecticut Air National Guard.

---

[12] http://usmilitary.about.com/library/milinfo/blferes.htm.

[13] Associated Press, 2005: Journal Releases Vioxx Study. CNN.com at (http://www.cnn.com/2005/HEALTH/01/25/vioxx.study.ap/).

[14] (Merck & Co., Annual report, 2003).

Time Line: Development and use of the Anthrax Vaccine

and the Anthrax Vaccine Immunization Program

Compiled by Major Thomas Rempfer and Lt. Col. Russell Dingle, Connecticut Air National Guard

1. **January 1955.** An anthrax vaccine supplied by the U.S. Army Chemical Corps was used in the first human field trial. During this clinical trial five workers contracted inhalation anthrax and four died in the first anthrax epidemic of the 20th Century.[i]

2. **September 1965.** A human anthrax vaccine patent was awarded to Milton Puziss and George Wright, representing the U.S. Army.[ii] (The vaccine described in this patent was materially different from the vaccine used in the 1955 to 1959 New Hampshire field trial.)

3. **July 1967.** An application is made with the Health Education and Welfare's Division of Biologic Standards to license an anthrax vaccine based on the patented vaccine production method.[iii]

4. **July 1967.** First required annual progress report submitted to the Division of Biologic Standards.[iv]

5. **February 1969.** The Division of Biologic Standards recommended license approval, but noted that clinical data establishing efficacy had not been submitted and requested data be gathered to establish efficacy.[v]

6. **November 1970.** The Division of Biologic Standards approved the anthrax vaccine.[vi]

7. **February 1972.** Final Progress Report on the anthrax vaccine was submitted to the Division of Biologic Standards.[vii] (Data establishing efficacy of this vaccine as requested in February 1969 had yet to be generated, collected, submitted or reviewed by the Division of Biologic Standards.)

8. **June 1972.** The responsibility of regulating biologic products, including vaccines, is transferred from the Division of Biologic Standards to the Food and Drug Administration.[viii]

9. **August 1972.** The Food and Drug Administration announced a review of all products transferred from the Division of Biologic Standards for safety, effectiveness and labeling.[ix] AVA was one such product.

10. **May 1985.** The DoD (through the Department of the Army) issued a Request for Proposals (DAMD17-85-R-0078) to the pharmaceutical industry soliciting the development of a new anthrax vaccine. The reasons stated in the Request for Proposals was that there was no vaccine in current use that safely and effectively protects military personnel against exposure to anthrax and that the current anthrax vaccine was highly reactogenic, required multiple boosters to maintain immunity, and may not protect against all strains of anthrax.[x]

11. **December 1985.** The review required by the Food and Drug Administration in 1972 was published in the Federal Register as a Proposed Rule. The review panel recommended that AVA be placed in Category I as safe, effective and not mislabeled. The review panel did note the lack of efficacy data: "*the vaccine…has not been employed in a controlled field trial.*" The panel also noted the inability to determine the vaccine's use in preventing inhalation anthrax: "*efficacy against inhalation anthrax is not well documented . . . no meaningful assessment of its value against inhalation anthrax is possible due to its low incidence.*" Finally, based on the extremely limited use of the vaccine the panel felt the possible benefit outweighed the risk: "*In general, safety of this product is not a concern*

especially considering its very limited distribution and the benefit-to-risk aspects of occupational exposure in those individuals for whom it is indicated."[xi] This panel also found the dosage of the anthrax vaccine to be incorrect, and recommended a correction to the labeling to only 3 shots. The FDA has not finalized the anthrax vaccine license proposed rule.

12. **February 1986**. Dr. Gregory B. Knudsen published an article in Military Medicine on anthrax in man. Knudsen concluded that by extrapolating animal studies, which demonstrate that vaccination is not protective against all anthrax strains or concentrations to humans, we can expect that the vaccine will not protect humans against all strains or concentrations as well.[xii]

13. **March 1988**. USAMRIID researcher Bruce Ivins wrote in the European Journal of Epidemiology of the inability of the anthrax vaccine to adequately protect against certain strains of anthrax.[xiii]

14. **May 1989**. When asked by the U.S. Senate Committee on Governmental Affairs to explain the DoD's assessment that the U.S. cannot adequately defend its service personnel against anthrax, Assistant Secretary of Defense Robert B. Barker answered,

    "The assessment in the 1986 report is accurate. Current vaccines, particularly the anthrax vaccine, do not readily lend themselves to use in mass troop immunization for a variety of reasons: ...a higher than desirable rate of reactogenicity, and, in some cases, lack of strong enough efficacy against the aerosol route of exposure."[xiv]

15. **March 1990**. Army Colonels E.T. Takafuji and P. K. Russell published an article describing the human anthrax vaccine as a "*limited use vaccine*" and an "*unlicensed experimental vaccine*". [xv]

16. **September 1990**. The anthrax vaccine producer, then the Michigan Department of Public Health (MDPH), increased its production capacity and modified its production process to accommodate DoD needs. These production changes included changing the filtration system, using different fermentation equipment, different sterilization procedures, chill tanks, etc. FDA was eventually notified of some of these changes after the fact. FDA was unaware of others until Congressional and GAO inquires were made in 2000. DoD involvement to some unknown degree is apparent from a review of declassified documents.[xvi]

17. **October 1990**. US Army medical research personnel from Fort Detrick, Maryland determined that the changes in the anthrax vaccine manufacturing process produced a 100-fold increase in protective antigen levels of the vaccine.[xvii]

18. **May 1993**. First in a series of FDA inspections of the anthrax vaccine manufacturing facilities began noting serious deviations from regulations and that the vaccine manufacturer was in violation of current Good Manufacturing Practices (cGMP).[xviii]

19. **1994**. U.S. Army officer and researcher Col. Arthur M. Friedlander co-authored a chapter on the anthrax vaccine for the medical reference textbook "Vaccines". Friedlander wrote that:

    "No assessment of the effectiveness of the vaccine against inhalation anthrax could be made because there were too few cases. ... There have been no controlled clinical trials in humans of the efficacy of the currently licensed U.S. vaccine. ... The current vaccine against anthrax is unsatisfactory for several reasons. The vaccine is composed of an undefined crude culture supernatant absorbed to aluminum hydroxide. There has been no quantification of the protective antigen content of the vaccine or of any of the other constituents, so the degree of purity is unknown. ... The vaccine is also less than optimal in that six doses are required over 18 months, followed by annual boosters. There is also evidence in experimental animals that the vaccine may be less effective against some strains of anthrax."[xix]

20. **June 1994**. FDA inspection of manufacturer noted non-compliance with regulations and cGMPs.[xx]

21. **December 1994**. Senate Veterans Affairs Committee determined that the use of the anthrax vaccine during the Gulf War was investigational. Future Army Surgeon General Ronald Blanck testified that the anthrax vaccine should be considered a possible cause of Gulf War Illness.[xxi]

22. **April 1995**. FDA inspection of manufacturer noted continued non-compliance with regulations and cGMPs.[xxii]

23. **August 1995**. FDA issued a warning letter to the anthrax vaccine manufacturer for their continuing failure to comply with the regulations and remedy the deficiencies noted in the various inspections. The manufacturer was warned that failure to promptly correct those deviations could result in regulatory action to include seizure, injunction, and license suspension.[xxiii]

24. **October 1995**. The U.S. Army contracts with Science Applications International Corporation (SAIC) to develop a plan to obtain FDA approval for a license amendment for the anthrax vaccine. The license amendment would enable the manufacturer of the vaccine to indicate that the anthrax vaccine was effective against "*inhalation anthrax*." The SAIC license amendment plan stated that the anthrax vaccine was not licensed as protection for aerosol anthrax exposure (inhalation anthrax) as expected in a biological warfare environment.[xxiv]

25. **October 1995**. The Army's newly formed Joint Program Office for Biological Defense (JPOBD) met to discuss the proposed anthrax vaccine license amendment. The participants noted that studies showed the vaccine to be effective for tannery workers, but that there was insufficient data to demonstrate protection against inhalation anthrax.[xxv]

26. **February 1996**. A U.S Army representative was presented with a report on the anthrax vaccine manufacturer, which indicated equipment in use had not been approved by FDA and could result in severe consequences if FDA found out.[xxvi]

27. **September 1996**. The anthrax vaccine manufacturer submitted an investigational new drug application for the anthrax vaccine to the FDA (IND #6847). At this point the anthrax vaccine was now considered an investigational new drug when used for the purpose described in the application, i.e. "*inhalation anthrax*".[xxvii]

28. **November 1996**. FDA inspected the anthrax vaccine manufacturer and noted continued non-compliance with regulations and cGMPs.[xxviii]

29. **March 1997**. FDA issued a Notice of Intent to Revoke letter to vaccine manufacturer for failure to remedy regulatory deficiencies and non-compliance.[xxix]

30. **March 1997**. DoD Joint Program Manager for Biological Defense briefed the Deputy Secretary of Defense concerning the anthrax vaccine production problems. A worst-case scenario was laid out, which threatened the as yet to be announced anthrax vaccination program. The AVIP was revealed as the launch program for a larger initiative called the Joint Vaccine Acquisition Program (JVAP), which would field up to 18 more biowarfare vaccines[xxx]

31. **March 1997**. Acting FDA Commissioner Dr. Friedman wrote a personal memo to DoD Assistant Secretary of Defense (ASD) for Health Affairs, Dr. Joseph, which accepted DoD's new position that the anthrax vaccine could be used for inhalation anthrax. The IND application, which requested that the new use be added to the product label, was not

addressed. Friedman's memo or opinion had no legal authority. The Code of Federal Regulations at 21 C.F.R. § 10.85 -- Advisory Opinions – explained why the March 1997 letter by FDA Lead Deputy Commissioner was legally irrelevant – yet the DoD used this memo to justify product approval for an experimental use.[xxxi] In his memo to the DoD, Dr. Friedman wrote that, "*Results from animal challenge studies have also indicated that pre-exposure administration of anthrax vaccine protects against inhalation anthrax.*"[xxxii]

32. **December 1997**. A Joint Program Office for Biological Defense report continued to note that "*Anthrax and Smallpox are the only licensed vaccines that are useful for the biological defense program, but they are not licensed for a biological defense indication.*"[xxxiii]

33. **December 1997**. FDA interoffice memorandum indicated that the vaccine manufacturer routinely redated vaccine without proper authority or approval.[xxxiv]

34. **December 1997**. DoD announced a multi-service vaccination program for all active duty, Reserve and National Guard service members using the anthrax vaccine as a preventative measure for inhalation anthrax.[xxxv]

35. **February 1998**. FDA inspected the anthrax vaccine manufacturer, found multiple deviations from cGMPs and determined that the manufacturing process was no longer validated.[xxxvi] Manufacturer "voluntarily" quarantined 11 of 19 Lots of the anthrax vaccine.

36. **February 1998**. Within one day of the FDA inspection, which revoked the validation of the anthrax vaccine manufacturing process, an independent expert completed a four-point review of the AVIP, mandated by Defense Secretary Cohen.[xxxvii] Later this expert admitted in a letter to Congressional investigators he had no expertise in anthrax. One aspect of the four-point review included supplemental testing of the vaccine, which DoD officials later admitted to Congressional investigators was suspended due to "*inconsistencies.*"[xxxviii] Internal documents later revealed that testing results where "*all over the board,*" and were terminated to preclude having to report the problems to FDA.

37. **September 1998**. Army Secretary Louis Caldera authorized indemnification of the manufacturer stating:

> "*the obligation assumed by MBPI under this contract involves* ***unusually hazardous risks*** *associated with the potential for adverse reactions in some recipients and the possibility that the desired immunological effect will not be obtained by all recipients. ...[T]he size of the proposed vaccination program may reveal unforewarned idiosyncratic adverse reactions. Moreover, there is no way to be certain that the pathogen used in tests measuring vaccine efficacy will be sufficiently similar to the pathogen that US forces might encounter to confer immunity.*"[xxxix]

38. **1999**. New Edition of the civilian medical textbook "Vaccines" printed with minor changes to the anthrax vaccine chapter.[xl] 1994 chronology, verbiage and assessments of the unsatisfactory nature of the vaccine by Friedlander and Brachman remain unchanged.

39. **1999**. 10 U.S.C. § 1107 became law. 10 U.S.C. § 1107 provided that investigational new drugs or drugs unapproved for their intended uses may not be given to members of the Armed Forces without their prior consent except in the case of a waiver by the President of the United States. 10 U.S.C. § 1107 reiterated and codified language already established in federal and military regulations.[xli]

40. **January 1999**. A British journal, The Lancet, published a study establishing a link between Gulf War vaccinations and Gulf War Illness.[xlii]

41. **January 1999**. Investigational New Drug application #6847 is updated with the FDA's Center for Biologics Evaluation and Research. The primary reason, and the only one listed on the application update, was for a clinical indication for "*inhalation anthrax*" on the anthrax vaccine product label.[xliii]

42. **March 1999**. Hearings on AVIP began in House Government Reform Committee, the Government Reform Committee Subcommittee on National Security, International Relations and Veterans Affairs, the House Armed Services Committee and the Senate Armed Services Committee. Nine hearings were conducted in 1999.[xliv]

43. **March 1999**. The General Accounting Office (GAO) testified and issued the first of many critical reports on the anthrax vaccine and the AVIP.[xlv]

44. **March 1999**. Dr. Meryl Nass reviewed the anthrax vaccine in a biologic warfare context in Infectious Disease Clinics of North America concluding that when the DoD controls all steps in the vaccine development and production process, along with being the employer of both physicians and the servicemember recipients, there will be problems, including ethical conflicts, insufficient testing of products, inadequate quality control, inadequate record keeping, and lack of proper surveillance for side effects.[xlvi]

45. **April 1999**. DoD admitted the use of the anthrax vaccine was only routine in military research laboratories and that they did not intend to mislead or confuse the public with their previous pronouncements of routine civilian veterinarian use. DoD modified tri-fold brochure replacing "*civilian*" with "*at risk*".[xlvii]

46. **May 1999**. Internal DoD correspondence by Brigadier General Cain, following Congressional testimony, revealed:

    "*... two key areas we came up flat were the GAO's assertion that #1, the anthrax vaccine licensed was NOT the one tested and #2, how can DoD say that reported desert storm illnesses were not cause (sic) by the anthrax vaccine when we have no record of who received the shots. If we cannot answer these questions we (DoD & the Administration) are in big time trouble.*"[xlviii]

47. **September 1999**. President Clinton issued Executive Order (EO) 13139. EO 13139 stated that before administering an investigational drug, or a drug unapproved for its intended use, to members of the Armed Forces, the DoD must obtain informed consent from each individual unless the President of the United States signs a waiver of this requirement. This EO reiterated the requirements already codified in US law.[xlix]

48. **October 1999**. The FDA and the DoD proposed to amend the law in a proposed rule, "*New Drug and Biological Drug Products; Evidence needed to Demonstrate Efficacy of New Drugs for Use Against Lethal or Permanently Disabling Toxic Substances When Efficacy Studies in Human Ethically Cannot be Conducted*".[l] This amendment would allow evidence of effectiveness derived from appropriate studies in animals, without adequate and well-controlled efficacy studies in humans, to be used to earn full approval for vaccines or drugs for soldiers.[li]

49. **2000**. The House Government Reform Committee, the Government Reform Committee Subcommittee on National Security, International Relations and Veterans Affairs, the

House Armed Services Committee and the Senate Armed Services Committee held a total of ten hearings.[lii]

50. **2000**. GAO testified and issued seven more critical reports on the AVIP and the threat of weaponized anthrax.[liii]

51. **February 2000**. After eight hearings the Committee on Government Reform issued its findings in a report – Unproven Force Protection. They found the use of the anthrax vaccine by the military was experimental, that the AVIP lacked a consistent standard of care, and was designed to reach far beyond those at risk.[liv] The DoD refused to modify the AVIP in order to comply with FDA regulations and US law as recommended by the Government Reform Committee.

52. **March 2000**. The Institute of Medicine issued a Letter Report assessing the safety of the anthrax vaccine and concluded there was a paucity of data on both the safety and efficacy of the anthrax vaccine.[lv]

53. **March 2000**. FDA admitted to Representative Metcalf of WA in a written response that trace amounts of an unapproved adjuvant, squalene, was found in all anthrax vaccine Lots tested. Previously, DoD had categorically denied that the anthrax vaccine has ever contained squalene.[lvi]

54. **April 2000**. An article reviewing the anthrax vaccine in the journal "Infectious Diseases" acknowledged that "*The pre-clinical, clinical, pharmacological and safety data that would be required for a new product to be licensed today [was] never generated.*"[lvii]

55. **May 2000**. A Canadian Judge, Col. Guy Brais, dismissed a case against a Canadian soldier, Michael Kipling, who refused the anthrax vaccine. The Judge deemed the anthrax vaccine was "*unsafe.*"[lviii]

56. **July 2000**. DoD slowed AVIP due to a lack of vaccine supply.[lix]

57. **October 2000**. GAO issued a report titled: Preliminary Survey of Guard and Reserve Pilots and Aircrew, 01-92T. The report's abstract states:

    "Many questions have been raised about the program since DoD began vaccinating its 2.4 million active duty and reserve members in 1998. A major concern has been the program's effect on the National Guard and Air Force Reserve's retention of trained and experienced personnel. A questionnaire sent to 1,253 randomly selected Guard and Reserve pilots and others revealed that the anthrax immunization was a key reason these individuals left or otherwise changed their military status. Since September 1998, an estimated 25 percent of the pilots and aircrew members of the Guard and Reserve in this population transferred to another unit, left the military, or moved to inactive status."

58. **November 2000**. The American Journal of Epidemiology published a study of Kansas's veterans, which described the Gulf War Illness symptoms of servicemembers who didn't deploy to South West Asia but received the anthrax vaccine.[lx]

59. **December 2000**. The Center for Disease Control's Advisory Committee on Immunization Practices issued a report on the use of the anthrax vaccine. They did not recommend the vaccine for emergency first responders, federal responders, medical practitioners or private citizens. Further, the Committee determined that the target population could not be predetermined and that the risk of exposure to anthrax could not be calculated.[lxi]

60. **2001**. GAO testified and issued six critical reports on the AVIP and the threat of weaponized anthrax.[lxii]

61. **June 2001**. Senator Daschle, the Senate Majority Leader, and Representative Gephardt, the House Minority Leader, wrote a joint letter to Secretary of Defense Rumsfeld questioning the anthrax vaccine program and the punishments of soldiers.[lxiii]

62. **June 2001**. DoD suspended the AVIP due to a lack of vaccine.[lxiv]

63. **August 2001**. DoD Undersecretaries submitted recommendations to Secretary of Defense Rumsfeld to minimize use of the current anthrax vaccine, develop a new vaccine, procure biodetection systems, and institute a coherent process for dealing with biological warfare threats in the future.[lxv]

64. **September 2001**. Gen. Shelton, Chairman of the Joint Chiefs of Staff, responded to the Undersecretaries' recommendations, adamantly insisted that the AVIP was supported by his subordinate commanders and was the "*centerpiece*" for biological defense.[lxvi]

65. **October 2001**. Anthrax, delivered through the US postal service, arrived in Senator Daschle's office on the 15th of October. One business day earlier BioPort applied for an expedited approval of its anthrax manufacturing line. Senator Daschle ultimately recommended his staff take the anthrax vaccine. It is unknown if Senator Daschle ever followed up on the anthrax vaccine questions presented to the DoD several months earlier.

66. **October 2001**. A Citizen Petition was filed with the FDA requesting they declare the anthrax vaccine adulterated based on the unapproved and illegal manufacturing alterations, and revoke the anthrax vaccine manufacturer's license based on meeting the threshold of license revocation on both the scientific and regulatory grounds.[lxvii] The petition also covered the fact that the DoD's contracts for the anthrax vaccine were in conflict with FDA policy guidance, since the manufacturer had received warning letters and other adverse regulatory actions, and the fact that the FDA proposed rule noted that the vaccine regimen was intended to be only 3 shots, not 6.[lxviii]

67. **October 2001**. DoD reported to Congress on their co-sponsorship of the proposed rule to change the law to allow licensure of biological warfare defensive protection measures based on animal data. The proposed rule was attached to the 2001 Bioterrorism bill that passed without dissent.[lxix]

68. **November 2001**. An article in The Lancet reviewed how early and aggressive post exposure treatment with antibiotics saved the lives of several anthrax letter victims.[lxx]

69. **November 2001**. A trade journal article, Nursing Times, published an article expressing reservations on recommending the vaccine to their members based on published reports of adverse reactions.[lxxi]

70. **December 2001**. An article published by members of the US Army expressed the belief that the vaccine was effective, in contrast to previous DoD admissions that the vaccine was not effective against all known strains. The article purported to review the adverse reaction data, and minimized the deleterious effects of the vaccine on the military population. These findings were refuted several months later by a civilian review of the same data.[lxxii]

71. **January 2002**. The anthrax vaccine manufacturer's license to manufacture and distribute vaccine (under a new trademark, BioThrax) was approved after the FDA accepted the expedited application. A review of FDA's newly approved anthrax vaccine product label

revealed systemic adverse reaction rates now published at 5 to 35% based on post-surveillance studies, which was up to 175 times or 17,500% higher than the original 0.2% on the old product label when the AVIP was announced in 1997. The new anthrax vaccine product label also listed six reported deaths including cardiac arrest, myocardial infarction, aplastic anemia, central nervous system (CNS) lymphoma. Birth defects were also listed based on a US Navy retrospective study. The FDA revised the product labeling, confirming positive risk of birth defects based on human data, and downgraded the vaccine to Category D. Approximately 40 serious adverse events were now on the product label including: cysts, sepsis, angioedema, asthma, aplastic anemia, lymphoma, leukemia, vascular disease, systemic lupus, multiple sclerosis, arthritis, Guillain-Barré syndrome, immune deficiency, seizures, tremors, facial palsy, hearing and visual disorders, meningitis, encephalitis, atrial fibrillation, spontaneous abortion, liver abscess, fatigue, mood-cognition, musculoskeletal disorder.[lxxiii]

72. **January 2002.** A paper establishing the existence of squalene in the anthrax vaccine was published. Squalene was a substance known to be present in virtually every person with Gulf War Illness.[lxxiv]

73. **January 2002.** 24 January 2002 Congressional testimonial exchange with GAO investigators revealed that the DVA had data linking anthrax vaccine to GWI, but data was not released to the public:

    Mr. Shays. "*OK. In your testimony, you said according to studies in both the U.K. and the U.S. veterans of the Gulf war who reported receiving biological warfare inoculations for anthrax or other threats were more likely to report a number of symptoms than non-Gulf war veterans who did not report receiving such inoculations. This pattern was observed in data collected in the United Kingdom in an unpublished data collected by the U.S. Department of Veterans Affairs. Why do you think the VA has not published its finding regarding the link between advance symptoms and the anthrax vaccination?*"

    Ms. Kingsbury. "*I don't know why they didn't publish it. We are aware of it. We have asked them. They said to us what they said to you this morning, things about the analysis not being completed and that sort of thing. I'm not in a position to second-guess it. We consider it to be valid, useful information that ought to be in the public domain.*"[lxxv]

74. **March 2002.** The Institute of Medicine issued a Congressionally mandated, DoD funded, report on the anthrax vaccine. The report recommended the vaccine for soldiers, and was authored by the same experts that had been involved with the DoD's anthrax vaccine program and other experts that were involved with the DoD's original anthrax vaccine trial in 1957[lxxvi] The report was used to justify the subsequent relaunch of the AVIP, but held no regulatory relevance.

75. **March 2002.** A civilian review of adverse reactions was published showing a significant increase in joint symptoms following vaccination with AVA when compared to joint symptoms following vaccination with hepatitis A and Td.[lxxvii]

76. **April 2002.** A study of over 900 Reserve members showed that Gulf War veterans were more likely to report poor health than non-Gulf War veterans, including veterans who received the anthrax vaccine who reported more reactions to vaccines than those who did not receive the anthrax vaccine.[lxxviii]

77. **April 2002**. A published article demonstrated that the anthrax vaccine caused statistically significant adverse reactions ranging from arthralgia, to vasculitis, to joint disease, to gastrointestinal disease and weight loss.[lxxix]

78. **June 2002**. DoD formally restarted the AVIP.[lxxx]

79. **July 2002**. DoD Inspector General (IG) referred an amended complaint (#84142) to the Defense Criminal Investigative Service (DCIS) concerning the anthrax vaccine program. MG Randall West, the Office of the Secretary of Defense officer responsible for the AVIP, was tasked with investigating a previous, similar complaint. Following his investigation, he dismissed the complaint. The original complaint included concerns about questionable testimony to the US Senate, and a Canadian Judge concerning the IND application by military officers. The amended complaint added additional questionable testimony to the House of Representatives, and broader concerns about the adulteration of the vaccine, the failure to properly study the vaccine as a possible cause of Gulf War Illness (GWI), and concerns about the willfully blind nature of the DoD's conduct despite soldiers documenting the risks of the vaccine.[lxxxi] The new complaint's investigation is pending.

80. **July 2002**. Article by Kansas State University scientists critiqued the National Academies of Sciences Institute of Medicine Report, which found the anthrax vaccine safe and effective, based on its "*omissions and limitations*." The critique explained that the report "*ignored evidence of several recent research studies from three different nations that have implicated vaccines, often including anthrax vaccine, in the epidemiology of Gulf War illnesses.*"[lxxxii]

81. **August 2002**. FDA responded to a Citizen Petition filed under Title 21 of the US Code. The response confirmed the fact that FDA never finalized the anthrax vaccine license as required by law, and that none of the old anthrax vaccine would be released.[lxxxiii]

82. **October 2002**. Air Force Chief of Staff General Jumper promulgated AVIP policy and guidance for all active duty and reserve units. The policy stated that, "*The vaccine must be given in accordance with the ... dosing schedule, as approved by the Food and Drug Administration.*" Notwithstanding the CSAF's guidance to follow the licensed vaccination schedule, Paragraph 4c of Annex B of the plan stated: "*Personnel whose vaccination series was interrupted during the previous AVIP slowdown will not need to repeat any doses already received in the vaccine series or receive extra doses. Once these individuals are identified as requiring the vaccine, they will just continue with the next dose in the series.*"[lxxxiv]

83. **October 2002**. GAO's final report[lxxxv], Survey of Guard and Reserve Pilots and Aircrew, report #02-445, revealed on page 5 that:

> *"The systemic reaction rate reported through the survey represents a level more than a hundred times higher than the 0.2 percent published in the product insert. We were unable to determine why the AVIP reaction rates so exceeded the product insert rates for the vaccine as approved in 1970. However, we found two studies conducted by DoD that looked at the short-term safety of the vaccine -- one in Korea and one in Hawaii. Both reported reaction rates similar to those reported in our survey and disclosed a markedly higher rate of reaction for female shot recipients. Since we first reported these results from our survey in September 2000, the manufacturer's product insert has been revised to include the adverse reaction rates reported in post licensure survey studies."*

84. **October 2002 Continued**. GAO report #02-445 also revealed on pg. 23 that:

> *"In addition, although DoD has maintained from AVIP's outset that the anthrax vaccine is very safe and causes minimally adverse effects, our survey disclosed that a significantly large number of vaccine recipients reported experiencing adverse events. Further, the results of two DoD studies on anthrax vaccine reactions, both of which used active monitoring systems, as opposed to a passive system such as VAERS, for gathering information on adverse events, are consistent with and support the results of our survey. The rates disclosed in the survey and the DoD studies are each significantly higher than those stated in the vaccine product insert until recently. Such marked variances from the product insert data suggest the possibility of change in the composition of the vaccine from the vaccine originally approved in 1970."*

85. **October 2002 Continued**. The GAO report #02-445 abstract summarized the readiness implications of the AVIP:

> *"GAO reviewed the views of pilots and aircrew members of the Air National Guard and Air Force Reserve regarding the Anthrax Vaccine Immunization Program (AVIP) of the Department of Defense (DoD). ...Between September 1998 and September 2000, 16 percent of the pilots and aircrew members of the guard and reserve had (1) transferred to another unit (primarily to nonflying positions to avoid or delay receiving the anthrax shots), (2) moved to inactive status, or (3) left the military. Additionally, one in five of those still participating in or assigned to a unit in 2000 indicated their intention to leave in the near future. At the time of the survey, two-thirds of the guard and reserve pilots and aircrew members did not support DoD's mandatory AVIP or any future immunization programs planned for other BW agents. However these negative views did not appear to indicate a general anti-vaccine bias. On the basis of the survey, GAO estimated that 37 percent of the guard and reserve pilots and aircrew members had received one or more anthrax shots as of September 2000. Of these recipients, 85 percent reported experiencing some type of reaction. ..."*

86. **February 2003**. FDA approved pyridostigmine bromide (PB) for use to protect soldiers from chemical weapons. The approval marked the first application of the "animal efficacy rule" proposed by the DoD in October 1999, reported to Congress in October 2001 and passed in to law in the summer of 2002 following passage of the Bioterrorism bill. Opponents of the use of PB referenced a 1999 study by the RAND Corporation and a 2000 report by the Institute of Medicine that concluded PB could not be ruled out as cause of Gulf War Illness. Evidence of efficacy inferred from animal data and the unresolved issues pertaining to Gulf War Illness were identical to that of the anthrax vaccine.

87. **February 2003**. United States District Court ruling, for a US Army soldier's discharge upgrade case, cautioned that:

> *" ... It is important for the parties and the public to understand exactly what the Court is ruling. The Court is not passing on the merits of the anthrax program. The plaintiff has raised significant questions about that program. If the Court were reviewing the program, the Court would be very concerned about the question that the plaintiff has raised. Title 10 United States Code*

Section 1107 provides that whenever the Secretary of Defense requests a member of the armed forces to receive an investigational new drug, the Secretary must provide a member with notice about the investigational nature of the drug and require the member's consent prior to administration ... There have been no tests showing that the vaccine is effective at protecting human beings from exposure to inhalation anthrax, although animal studies by the Army exist. The Court will not substitute its opinion for that of the Army, but it will not review the matter. And its ruling today should not be understood as an approval of what the military is doing in this case. The military will be held accountable to the public if it is using its own soldiers as guinea pigs to determine whether the anthrax vaccine has long-term health consequences and whether it protects against airborne anthrax. Those decisions, are, as I said, decisions that are committed to the Executive Branch of the Government. The Court neither approves nor disapproves of those decisions, because it is not the function of the Court to do that. Those decisions will be debated, and ultimately the Executive Branch will be held accountable to the public for those decisions. And that is the way the system of government works. . . "[lxxxvi]

88. **March 2003.** Case 1:03-cv-00707-EGS JOHN DOE et al v. RUMSFELD et al filed in the United States District Court for the District of Columbia requesting that a federal judge declare that the anthrax vaccine an experimental drug and illegal. A separate motion was also filed seeking a Temporary Restraining Order or Preliminary Injunction against the defendants to prevent further anthrax inoculations without informed consent or a presidential waiver according to law and Executive Order. Specific aspects of the suit include:

    a. FDA Failure to properly finalize the anthrax vaccine license;

    b. Anthrax vaccine experimental use for inhalation anthrax;

    c. And DoD deviation from anthrax vaccine license requirements.

89. **March 2003.** Additional multiple Federal lawsuits were filed against the manufacturer for wrongful injury, with specific counts including:

    a. Negligence

    b. Breach of Warranties

    c. Breach of the right to be treated with essential human dignity

    d. Strict products liability

    e. Fraud

    f. Deprivation of civil rights and

    g. Spouse's loss of assistance, companionship and consortium.

[i] See supra note 23.

[ii] U.S. Patent No. 3,208,909; 28 September 1965.

[iii] Michigan Department of Public Health application to the Public Health Service Division of Biologic Standards, 11 July 1967.

[iv] Ibid.

[v] Pittman M, Division of Biologic Standards Memorandum dated 10 February 1969.

[vi] Health, Education and Welfare letter to Michigan Department of Public Health, dated 10 November 1970.

[vii] Michigan Department of Pubic Health Final Report, dated 3 February 1972.

[viii] Federal Register at 37 FR 12865, 29 June 1972.

[ix] Federal Register at 37 FR 16679, 18 August 1972.

[x] DoD Request for Proposals (RFP) -- DAMD17-85-R-0078. 16 May 1985.

[xi] Federal Register at 50 FR 51058, 13 December 1985

[xii] Knudsen GB. Treatment of Anthrax in Man: History and Current Concepts. Military Medicine, Vol. 151, No. 2 pp 71-77.

[xiii] Ivins BE, Welkos SL. Recent Advances in the Development of an Improved Human Anthrax Vaccine. European Journal of Epidemiology. Vol. 4 pp 12-19.

[xiv] Global Spread of Chemical and Biological Weapons. Hearings before the Committee on Governmental Affairs and its Permanent Subcommittee on Investigations. Senate Hearing 101-744.

[xv] Takafuji ET, Russell PK, Military Immunizations: Past, Present, and Future Prospects. Infectious Disease Clinics of North America. Vol. 4. No. 1 pp 143-58 1990

[xvi] Excerpts from DoD declassified chronology: "14 SEP 90 -- ... task from DJS to form a special group to develop proposed PA guidance for the BW Vaccination Program ... under the auspices of J-5 (Deputy Director for Political Military Affairs -- BG Jumper)...

21 SEP 90 – 'Special Topic' briefed in the TANK to the Operations Deputies by J-4 (RADM Smyth) and J-5 (BG Jumper) ... Bottomline: decision necessary were no longer "medical" in origin; rather were political, social, and military / operational. Also, no matter what decision made, insufficient vaccines (both AX and BT) to cover all US forces at risk existed.

25 Sep 90 -- AX Production Charts provided DJS with explanation regarding commencement of production ... 25 Oct 90 -- Memo from DDMR (ADM Smyth) on status of AX production ... 2 Nov 90 -- Third TANK informational briefing held with OPSDEPS and Joint Chiefs ... No change in threat; AX vaccine production has been maximized ...

9 Nov 90 -- Trip to Michigan Department of Public Health Lab (Lansing, MI) by J5 (BG Jumper, COL Fleming) and J4 (ADM Smyth, COL Fry). Purpose: Determine problems and prospects affecting production of BW vaccines. Visited Director of the Lab (Dr. George Anderson) and the Chief of Biologic Products Division (Dr. Robert Myers). -- Increases in AX vaccine production favorable. ... here is need for an additional fermentor however. -- MDPH has suspended production of BT vaccine in favor of AX vaccine.

9 Nov 90 -- J5 / DDPMA (BG Jumper) formed a working group consisting of DIA, J3, J4, J5 to assure accurate tracking of vaccine production. 16 Nov 90 -- BG Jumper provided summary of BW threat and general overview of US defensive capabilities (to include vaccines). Briefing showed existing inventories fell short of requirements in the near term.

16 Nov 90 -- COL Lewis furnished latest information on MDPH fermentor. New fermentor installed and pre-production testing is beginning. Provided to BG Jumper and DJS by DDMR. 19 Nov 90 -- ASD (HA) memorandum to SECARMY, "Expansion of Industrial Base for Biological Vaccine Production." ... on short term

production of AX and BT. -- Requested steps be taken on a priority basis to monitor ongoing efforts at MDPH (increased production by 20 Feb 91)...

19 Nov 90 -- Initial information on quantities of antibiotics (doxycycline, ciprofloxacin) ... furnished by COL Lewis to DDMR and BG Jumper.

21 Nov 90 -- DA OTSG sent tasking from SECARMY to form Task Force to evaluate ways to increase production of AX and BT vaccines. Implementation Working Group, chaired by BG Blanck, would provide weekly production reports to DASD (MR).

3 Dec 90 -- J5/BG Jumper outlined course of action needed prior to next TANK session. Need to push toward total integration of all planning efforts associated with BW defensive measures. ... VCSA has tasked Surgeon General to get plan together (public affairs, psyops, POLMIL, medical, doctrine). Draft memorandum to SECDEF prepared by J5 / COL Fleming requesting SECDEF direct accelerated procurement actions to improve the US biological defensive posture. Memorandum was not finalized.

10 Dec 90 -- Paper submitted to ADM Smyth and BG Jumper on "Rationale for Antibiotics in Prophylaxis Against Inhalation Anthrax" (Rhesus Monkey Paper). Research effort has been used in considering the use of antibiotics following exposure to AX and before initiation of symptoms. Only one monkey died following treatment with 30 days of Ciprofloxacin antibiotic.

14 Dec 90 -- Armed Forces Epidemiological Board met to consider the use of antibiotics as an adjunct in countering the threat of inhalation AX. 8 Mar 91 -- CENTCOM Surgeon msg (081808ZMar91), ... Also indicated vaccination programs for AX and Bot T discontinued due to diminished threat."

[xvii] Ezell JW, Abshire T. In Vitro Analysis of Michigan Department of Public Health Human Anthrax Vaccine, U.S. Army Medical Research Institute of Infectious Diseases, 25 Oct 1990, (unpublished)

[xviii] Form FDA 483 dated 4 May 1993.

[xix] Friedlander AM, Brachman PS, "Vaccines", ed. Plotkin and Mortimer, 1994 edition chapter 26.

[xx] Form FDA 483 dated 3 June 1994.

[xxi] Is Military Research Hazardous to Veterans' Health? Lessons Spanning Half a Century. S. Prt. 103-97, 8 December 1994.

[xxii] Form FDA 483 dated 23 April 1995.

[xxiii] FDA letter to Michigan Department of Public Health, dated 31 August 1995.

[xxiv] SAIC Corporation plan, 29 Sep 1995, enclosure to memorandum from Dr. Anna Johnson-Winegar (US Army) to Dr. Robert Myers (MDPH), US Army Medical Research and Material Command, Fort Detrick, Frederick, MD

[xxv] LTC David Danley, "Minutes of the Meeting on Changing the Food and Drug Administration License for the Michigan Department of Public Health (MDPH) Anthrax Vaccine to Meet Military Requirements", held on 20 Oct 1995 meeting; Joint Program Office for Biological Defense memorandum, 13 Nov 1995.

[xxvi] Kenimer Associates report to SAIC on trip to MDPH dated 6 February 1996.

[xxvii] Michigan Biologic Products Institute application to Dr. K. Zoon, Director, Center For Biologics Evaluation and Research, dated 20 September 1996.

[xxviii] Form FDA 483 dated 18 November 1996.

[xxix] NOIR letter from FDA to Michigan Biologic Products Institute dated 11 March 1997, available at http://www.fda.gov/cber/infosheets/mich-inf.htm

[xxx] http://www.defenselink.mil/pubs/prolif97/secii.html.

[xxxi] 21 CFR 10.85, "Advisory Opinions" -- See: http://frwebgate.access.gpo.gov/cgi-bin/get-cfr.cgi?TITLE=21&PART=10&SECTION=85&YEAR=1999&TYPE=TEXT -- "A statement made or advice provided by an FDA employee constitutes an advisory opinion only if it is issued in writing under this section. A statement or advice given by an FDA employee orally, or given in writing but not under this section or Sec. 10.90, is an informal communication that represents the best judgment of that employee at that time but does not constitute an advisory opinion, does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed."

[xxxii] 13 March 1997 memo from FDA's Dr. Friedman to DoD's ASD/HA Dr. Joseph.

[xxxiii] Industrial Capabilities Assessment, Summary Report for the Production of Anthrax Vaccine, Preliminary report prepared by the Joint Program Office for Biological Defense, Falls Church, VA, December 1997.

[xxxiv] Memorandum from Jeanne Novak (DVRPA) to M. Carolyn Hardegree (CBER) dated 10 December 1997.

[xxxv] See supra note 20.

[xxxvi] Form FDA 483 dated 4 February 1998.

[xxxvii] http://www.defenselink.mil/other_info/burrows.html, http://www.anthrax.osd.mil/resource/qna/ind_rev.asp#11, http://www.af.mil/news/Apr1998/n19980416_980507.html, http://www.defenselink.mil/news/Aug1998/t08171998_t814ntrx.html,

[xxxviii] http://www.house.gov/reform/ns/hearings/testimony/cain4-30.htm

[xxxix] SecArmy Memorandum of Decision, dated 3 September 1998.

[xl] Friedlander AM, Brachman PS, "Vaccines", ed. Plotkin and Mortimer, 1999 edition chapter 24.

[xli] 10 U.S.C § 1107. TITLE 10, Subtitle A, PART II, CHAPTER 55, Sec. 1107

[xlii] Unwin C, et al. Health of UK Servicemen Who Served in Persian Gulf War. The Lancet. Vol. 353 pp 169-178.

[xliii] IND 6847 update to FDA dated January 29, 1999 -- block 7 specifically and exclusively reads: "Indication(s) (covered by this submission) Inhalation Anthrax"

[xliv] 1999 hearings:

1. 24 March – Subcommittee on National Security, Veterans Affairs and International Relations; Oversight of the AVIP.
2. 2. 22 April – Subcommittee on National Security, Veterans Affairs and International Relations; Implementation of the Persian Gulf War Veterans' Act of 1998.
3. 3. 29 April - Subcommittee on National Security, Veterans Affairs and International Relations; Anthrax II – Efficacy of the Mandatory Vaccine
4. 4. 30 June - Subcommittee on National Security, Veterans Affairs and International Relations; Oversight of the DOD Sole Source Procurement.
5. 5. 21 July - Subcommittee on National Security, Veterans Affairs and International Relations; Anthrax Vaccine Adverse Reactions
6. 6. 29 September - Subcommittee on National Security, Veterans Affairs and International Relations; Impact of the AVIP on Reserve and Guard Units
7. 7. 30 September – House Armed Services Committee; DOD and the AVIP
8. 8. 12 October – Government Reform Committee; Defense Vaccines: Force Protection or False Security?
9. 9. 9 November - Subcommittee on National Security, Veterans Affairs and International Relations; Force Protection – Improving Safeguards of IND Drugs.

[xlv] GAO Reports from 1999 are available at www.gao.gov or NSIAD-99-5, NSIAD-99-148, NSIAD-99-214, NSIAD-99-226, NSIAD-00-48, NSIAD-00-36

[xlvi] Nass M. Anthrax Vaccine-Model of a Response to the Biologic Warfare Threat. Infectious Disease Clinics of North America. Vol 13. No. 1 pp 187-208

[xlvii] Army Times, April 5, 1999.

[xlviii] May 3, 1999 – email exchange between JPOBD BG Eddie Cain and Col John Wade, reference 29 APR 99 Congressional testimonies and an ongoing Congressional investigation of the AVIP.

[xlix] https://www.denix.osd.mil/denix/Public/Legislation/EO/note54.html

[l] http://www.fda.gov/cber/rules/lethtox.pdf,

[li] 21 CFR 314.126

[lii] 1. 2 February - Subcommittee on National Security, Veterans Affairs and International Relations; Gulf War Veterans Illnesses -- The Current Research Agenda

2. 13 April - Senate Armed Services Committee; Review of the DOD AVIP

3. 14 April - Senate Armed Services Committee; DOD's anti-biowarfare vaccine acquisition program

4. 24 May - Subcommittee on National Security, Veterans Affairs and International Relations; DOD Chemical and Biological Defense Program . Management and Oversight.

5. 21 June - Subcommittee on National Security, Veterans Affairs and International Relations; Force Protection - Current individual protective equipment.

6. 12 July - Senate Armed Services Committee; AVIP- The Threat, Effectiveness, Safety and Supply

7. 13 July – House Armed Services Committee; DOD and the AVIP

8. 27 September - Subcommittee on National Security, Veterans Affairs and International Relations; Gulf War Veterans-Linking Exposure to Illnesseses

9. 3 October – Committee on Government Reform; AVIP-What Have We Learned

10. 11 October – Committee on Government Reform; AVIP-What Have We Learned

[liii] GAO Reports available at www.gao.gov or NSIAD-00-157, NSAID-00-140, NSIAD-00-138, NSIAD-00-97, GAO-01-92T, GAO-01-21.

[liv] The Department of Defense Anthrax Vaccine Immunization Program - Unproven Force Protection. House Report 106-556. Available at House Report 105-556

[lv] Institute of Medicine Letter Report to MGen West on 30 March 2000 available at: http://www.nap.edu/html/anthrax_vaccine/

[lvi] HHS letter from Melinda K. Plaisier to Representative Metcalf, 20 March 2000.

[lvii] Turnbull PCB. Current status on immunization against anthrax: old vaccines may be here to stay for a while. Current Opinion in Infectious Diseases, Vol. 13, No. 2 pp 113-120.

[lviii] May 5, 2000; Canada News Briefs By The Associated Press -- Judge Agrees Anthrax Vaccine Unsafe; Halts Court Martial, WINNIPEG, Manitoba.

[lix] SecDef Cohen announcement available at http://www.defenselink.mil/news/Jul2000/n07112000_20007114.html

[lx] Steele L. Prevalence and Patterns of Gulf War Illness in Kansas Veterans: Association of Symptoms with Characteristics of Person, Place, and Time of Military Service. American Journal of Epidemiology, Vol. 152, No. 10 pp 992-1002.

[lxi] Hughes JM, Cohen ML. Use of the Anthrax Vaccine in the United States-Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2000;49(No. RR-15).

[lxii] GAO Reports available at GAO-01-13, GAO-01-915, GAO-02-38, GAO-02-181T, GAO-02-219T , GAO-02-445

[lxiii] Letter provided by Senate Majority Leader's office staffer Mr. Randy DeValk.

[lxiv] DOD announcement available at: http://www.defenselink.mil/news/Jun2001/n06112001_200106112.html

[lxv] DoD memo to SECDEF Rumsfeld dated 10 August 2001.

[lxvi] http://www.washingtonpost.com/wp-dyn/articles/A42952-2001Sep28.html

[lxvii] A Citizen Petition on lack of data and unapproved manufacturing changes – docket #01p-0471:
http://www.fda.gov/ohrms/dockets/dailys/01/Oct01/101501/101501.htm#_Toc527850400;
This Citizen Petition PDF can be reviewed at the following link:
http://www.fda.gov/ohrms/dockets/dailys/01/Oct01/101501/cp00001.pdf

[lxviii] Compliance Policy Guides Manual, Sec. 400.200, titled -- "Consistent Application of CGMP Determinations (CPG 7132.12), http://www.fda.gov/ora/compliance_ref/cpg/cpgdrg/cpg400-200.html" which states: "*CGMP deficiencies supporting a regulatory action also support decisions regarding non-approval of drug marketing applications, government purchasing contracts, candidates for MAC, etc. Therefore, the issuance of a warning letter or initiation of other regulatory action based upon CGMP deficiencies must be accompanied by disapproval of any pending drug marketing application, or government contract for a product produced under the same deficiencies.*"
Note: The FDA issued a Warning Letter to the anthrax vaccine manufacturer on August 31, 1995, and a Notice

of Intent to Revoke (NOIR) their license on March 11, 1997. A subsequent FDA inspection, conducted between February 4th and 19th of 1998, found that the previous deficiencies had not been corrected; all three inspections documented violations of current good manufacturing practices (cGMPs) required under federal law. These regulatory actions, until corrected, made the manufacturer subject to the restrictions contained in this government policy. On September 3, 1998, the FDA informed the new owner of the anthrax vaccine manufacturing facility, BioPort Corporation, that "the Notice of Intent to Revoke issued to MBPI on March 11, 1997 would effectively transfer with the issuance of the license to BioPort and would remain in effect until all compliance issues had been satisfactorily resolved." These deficiencies have still not officially been resolved, and most certainly were not when the DoD contracted for Anthrax Vaccine in 1998. These discrepancies are available at the following link:
FDA Warns Michigan Biologic Products Institute of Intention to Revoke License:
http://www.fda.gov/cber/infosheets/mich-inf.htm

[lxix] http://www.defenselink.mil/pubs/chem_bio_def_program/2001_CBDP_Annual_Report.pdf – ***"ISSUE:* DoD does not have a current approved mechanism for licensure of chemical and biological defense medical products *(i.e.*, drugs and vaccines) because legal and ethical constraints prevent adequate full testing in humans. *SOLUTION:* The FDA and DoD are working together to amend the Code of Federal Regulations to allow animal efficacy data to be used in lieu of large-scale human clinical efficacy trials.** This mechanism of licensure is vital to provide military service personnel with licensed products. This rule will also establish requirements for licensure and allow the DoD to plan and conduct the appropriate studies to obtain approval for the products planned for production and licensing. Requests for approval of each medical product will be reviewed on an individual basis."

[lxx] McCarthy M. Early and aggressive treatment saves US anthrax victims. The Lancet, Vol. 358 pp 1703

[lxxi] Munro R. When Immunity may not be safe. Nursing Times, Vol. 97, No. 44 pp 10-11

[lxxii] Pittman PR et al. Anthrax vaccine: short-term safety experience in humans. Vaccine, Vol. 20 pp 972-978.

[lxxiii] See supra note 34.

[lxxiv] Asa PB et al. Antibodies to Squalene in Recipients of Anthrax Vaccine. Experimental and Molecular Pathology, Vol. 73 pp 19-27.

[lxxv] http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=107_house_hearings&docid=f:82953.wais

[lxxvi] See supra note 3.

[lxxvii] Geier DA et al. Anthrax vaccination and joint related adverse reactions in light of biological warfare scenarios. Clinical and Experimental Rheumatology, Vol. 20, No. 2 pp 217-220

[lxxviii] Schumm WR et al. Self-Reported Changes in Subjective Health and Anthrax Vaccination as Reported by over 900 Persian Gulf War Era Veterans. Psychological Reports, Vol. 90 pp 639-653.

[lxxix] Geier DA et al. Smallpox and Anthrax in the United States. Mealey's Emerging Drugs & Devices, Vol. 7, No. 8 pp 26-30

[lxxx] See supra note 5.

[lxxxi] DoD IG complaint #84142, POC -- Mr. Traban, 860-424-9098.

[lxxxii] Schumm, Webb, Jurich, Bollman, Kansas State University. Psychological Reports, Volume 91, 2002, 187-191, "Comments on the Institute of Medicine's 2002 Report on the Safety of the Anthrax Vaccine."

[lxxxiii] http://www.fda.gov/ohrms/dockets/dailys/02/Sep02/091102/80027a9f.pdf

[lxxxiv] http://www.anthrax.mil/media/pdf/AFPlan.pdf.

[lxxxv] GAO-02-445, Report to Congressional Requesters, United States General Accounting Office, September 2002 ANTHRAX VACCINE GAO*s Survey of Guard and Reserve Pilots, and Aircrew - http://frwebgate.access.gpo.gov/cgi-bin/usetfp.cgi?IPaddress=162.140.64.21&filename=d02445.txt&directory=/diskb/wais/data/gao.

[lxxxvi] United States District Court for the District of Colorado Civil Action No. 00-N-1022, 2 FEB 2003; Jemekiah Barber vs. the United States Army, et al. The Court: *"... the issues in this case are beyond the purview of the federal judiciary and that the Court must decline review because the Department of Defense has wide latitude over military personnel decisions. ... The courts have little competence in the complex decisions as to the control*

of a military force, and such professional military judgments are more properly subject to civilian control of the Legislative and Executive Branches, which are directly responsible for the people ... the defendants concede that the plaintiff has sufficiently alleged that she suffered the deprivation of a constitutional right or that the military violated federal statutes for its own regulations..."

[Whereupon, at 12:32 p.m., the subcommittee was adjourned.]

○